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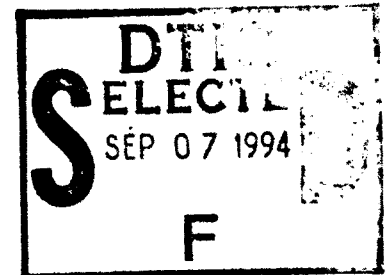
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SUBTITLE: 14-Day Toxicity Evaluation of N-Methyl-N, 2,4,6-Tetranitroaniline in  
Fischer 344 Rats

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## QUALITY ASSURANCE STATEMENT

The portions of this toxicology project performed and reported by Pathology Associates, Inc. has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Environmental Protection Agency. The following table is a record of the inspections/audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management and Study Director</u>
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## Compliance Statement

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 21 of the U.S. Code of Federal Regulations Part 792 issued August 17, 1989. All deviations from the protocol and/or GLPs are listed in Appendix J. There were no deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

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### **Study Timetable:**

Study Initiation: July 6, 1993

Initiation of Dosing: July 14, 1993

Completion of Necropsy: July 28, 1993

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## INTRODUCTION

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, it has been suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct (Burlinson, 1980). It is also found in aquatic systems and surface soils as a by-product of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of these compounds (Walsh and Jenkins, 1992).

Toxicity data on these compounds are limited. The oral LD<sub>50</sub> of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD<sub>50</sub> of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits were noted. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs (Fitzgerald et. al., 1992 a,b,c). Some of the toxicological effects of DNB are: formation of methemoglobin, testicular degeneration and reproductive failure, weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin (Von Burg, 1989). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Dermatitis, liver atrophy, spleen effects, headaches, weight loss and respiratory irritation were reported following tetryl exposure (U.S. EPA, 1990). Atmospheric concentration of 1.5 mg/m<sup>3</sup> or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in the Salmonella mutagenesis assay (McGregor et. al., 1989). TNB has also been shown to form adducts of blood proteins and tissue DNA in rats (Reddy et. al., 1991).

### Objective of the Study

This study was conducted in order to evaluate the toxicity of tetryl when administered in the diet for 14 days and to provide data to select doses for a 90 day subchronic study.

## MATERIALS AND METHODS

### Test Material Preparation

N-Methyl-N,2,4,6-Tetranitroaniline powder (CAS #479-45-8) 99.45% purity was prepared by Dr. W. Koppes of the Naval Surface Warfare Center. The purity was confirmed by the U.S. Army Biomedical Research and Development Laboratory and the U.S. EPA, Cincinnati. Certified powdered Purina Laboratory Chow 5002 was purchased (Ralston-Purina Co., St. Louis, MO) and stored at 4°C until used. Tetryl diets were prepared weekly. First, 3.75 g of tetryl was added to 50 g of powdered diet in a mortar and thoroughly ground with a pestle. This procedure was repeated to attain 7.5 g in the mixture. Afterwards 400 g of the diet was added and mixed for 30 minutes. Finally, the remaining diet (1000g) was added and mixed for 30 minutes in a mechanical mixer (Kitchen Aid, St. Joseph, MI) for uniform distribution of tetryl in the diet. This was verified by determining the tetryl concentration in the diet, taken from each of the 1 kg mixtures, by quantitative analysis done by HPLC. The premixed diet (5 g/kg) was further diluted with fresh powdered diet to obtain the desired tetryl concentration in the lower dose groups. The diet feeders were refilled twice a week and changed weekly.

Analyses of the tetryl-feed mixtures were carried out on acetone extracts of the mixtures, utilizing a Waters 600E chromatography system (Waters, Milford, MA), equipped with a 490E programmable multiwavelength detector, operating at 254 nm. The entire chromatography system was interfaced with a Berthold HPLC computer program, Version 1.65 (Berthold, Nashua, NH). The tetryl was eluted from a Zorbax C-8 column (9.4 mm x 25 cm) (MAC-DOD Analytical, Chadds Ford, PA) with a water-methanol gradient, at a flow rate of 3 ml/min. The gradient had an initial condition of 20% methanol which was increased in a linear fashion from 20% to 50% in 15 minutes and then to 65% in 25 minutes, and finally to 100% in 10 minutes. The column was washed for an additional 5 minutes and brought back to 20% methanol by reverse gradient and equilibrated for an additional 10 minutes at initial conditions before the next sample was injected. Working standards were prepared in Burdick and Jackson HPLC grade high purity methanol (Baxter, Obetz, OH). Analytical data of these mixtures is presented in Appendix I.

### Animals and Maintenance

Male and female Fischer 344 rats, confirmed free of viral antibodies, bacteria and parasites, were obtained from Charles River Laboratories, Kingston, New York. The animals, 7-8 weeks old and weighing approximately 140-175 g when delivered, were held for 1 week in quarantine prior to initiation of treatment. The animals were housed in a temperature (20-22°C) and humidity (40-60%) controlled room on a 12:12 hour light:dark cycle. For the study, they were housed individually in polycarbonate cages and water was administered ad libitum. Animal identification was done using electronic implants (Bio Medic, Maywood, NJ) with the rats assigned to control and treatment groups according to a computer-generated set of random numbers. The weight variation of the animals of each sex used did not exceed  $\pm 2$  s.d. of the mean weight at the time of delivery. The cages were identified with a color-coded identification card indicating the animal and treatment group. All aspects of the study

were conducted in compliance with the guidelines of the American Association for Accreditation of Laboratory Animal Care.

All rats were observed twice daily for physiological and behavioral responses as well as for mortality or morbidity. Food and water consumption were recorded twice weekly. Body weights were taken prior to the start of the study, once weekly during the study and at the final sacrifice.

A pilot palatability study was conducted at three tetryl dose levels (10, 3 and 1 g/kg diet) for two weeks. The data are presented in Appendix I1. Rats fed 10 g/kg diet consumed significantly less food therefore lower doses were selected.

### Experiment Design

Group	No. of Animals	Animal Nos.	Sex	Diet Concentration (mg tetryl/kg)
1	5	1-5	F	0
2	5	6-10	F	5000
3	5	11-15	F	2500
4	5	16-20	F	2000
5	5	21-25	F	1250
6	5	26-30	F	500
7	5	31-35	M	0
8	5	36-40	M	5000
9	5	41-45	M	2500
10	5	46-50	M	2000
11	5	51-55	M	1250
12	5	56-60	M	500

### Hematology and Clinical Chemistry

Hematology parameters were assessed using a Serono-Baker Hematology Analyzer, Model 9000, coupled to a computer running Labcat® software (Innovation Programming, Inc., Princeton, NJ). Total red and white blood cell counts, platelet count, differential leukocyte count, hemoglobin, and packed cell volume were measured and computed. Methemoglobin samples were analyzed on a IL 482 Co-Oximeter. Heinz bodies were determined using the crystal violet procedure (Lee et. al., 1993) with microscopic examination for positive cells (>5 Heinz bodies).

Clinical chemistry was performed using a Cobas Fara II centrifugal analyzer (Roche, Nutley, NJ) with a non-selective electrode (ISE) module. Clinical chemistry analytes included sodium, potassium, total protein, albumin, calcium, total bilirubin, blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, glucose and alkaline phosphatase.

### Statistical Evaluation

Males and females were considered separately in all statistical analyses. A one-factor (dose) analysis of variance (ANOVA) was used to analyze normally-distributed measures: body weights, organ weights, organ weight ratios, food and water consumption, hematology and clinical chemistry. When a treatment effect was noted

( $p \leq 0.05$ , F-test) the difference between the control and the treatment groups was probed using a multiple comparison procedure (Dunnett's t-test).

### Necropsy and Histopathology

Prior to necropsy, the animals were anesthetized with pentobarbital (60 mg/kg b.w., i. p.) and blood samples were collected via cardiac puncture after the body weight was recorded. Following euthanasia via exsanguination, all external surfaces, orifices, external surface of the brain, cervical tissues, all organs, and the thoracic, abdominal and pelvic cavities were examined for gross lesions.

During necropsy the following tissues were weighed: brain, liver, spleen, kidneys, adrenals, lungs, thymus, testes w/epididymides, ovaries, and heart.

The following tissues were harvested from each animal and preserved in 10% neutral buffered formalin:

skin	colon
mandibular and	cecum
mesenteric lymph nodes	rectum
mammary glands	liver
thigh muscle	pancreas
sciatic nerve	spleen
sternum	kidneys
femur with marrow	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs with bronchi	prostate
heart and aorta	testes, including epididymides
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity with turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord
ileum	

Subsequently, these tissues were trimmed, processed and embedded in paraffin. Blocks were sectioned at  $5\mu$  and slides were prepared and stained with hematoxylin and eosin. All tissues were examined in the high dose and control groups of both sexes. The spleen, testes and kidneys (males only) were identified as target organs and examined in the appropriate groups.

The inflammatory and degenerative lesions were graded according to severity using a scale of one to four (minimal, mild, moderate or marked). Data were tabulated according to individual animal and summarized by group. In addition, the gross

observations and microscopic diagnoses were correlated for each animal. Labcat histopathology software was used for data management.

#### Specimen, Raw data, and Final Report Storage

All tissue specimens, blocks and slides, raw data and final report will be placed in the U.S. EPA storage facility.

## **RESULTS**

#### Food and Water Consumption

Food and water consumption data are listed in Table 1, while individual data are presented in Appendix A. There were no significant changes in food and water consumption in any of the groups tested.

Using the food consumption data, the average daily tetryl dose levels received by group (see Experimental Design) are presented in Table 2. The average daily tetryl doses consumed (mg/kg b.w.) were 374, 179, 130, 83 and 32 for females and 350, 171, 121, 80 and 32 for males.

#### Body Weights, Organ Weights and Weight Ratios

The mean group values for body weights are listed in Table 3 while mean group organ weights (heart, brain, spleen, adrenals, thymus, ovaries/testes, kidneys, lungs and liver) are given in Tables 4 (females) and 5 (males). Mean group values for organ to body weight ratios are present in Tables 6 (females) and 7 (males). Individual body weights are found in Appendix B with individual organ weights present in Appendix C.

Significant decreases ( $p \leq 0.05$ ) from control body weights was noted in males receiving 5000 mg tetryl.

Organ weights as a percent of the total body weight were significantly ( $p \leq 0.05$ ) different from controls for the following organs:

Liver - The 5000 and 2500 mg tetryl dose groups (females) had increased values.

Kidneys - The 5000 mg tetryl dose group (males) had an increased value.

Spleen - The 5000 mg tetryl dose group (females) had an increased value.

#### Hematology

Hematology analyses performed were total white blood cell count (WBC), platelet count, red blood count (RBC), hemoglobin (HGB), hematocrit (HCT), reticulocytes, Heinz bodies, methemoglobin and differential leukocyte count. Group data are summarized in Tables 8 (females) and 9 (males). Individual data are listed in Appendix D.

1. WBC and Differential:

There were no significant differences in total white cell count or differential amongst the groups in either sex.

2. RBC:

There were no significant differences in the red blood cell count amongst the groups in either sex.

3. Hemoglobin:

A significant decrease ( $p \leq 0.05$ ) was noted in hemoglobin levels only in the 5000 and 2000 mg tetryl dose groups (females).

4. Hematocrit:

A significant decrease ( $p \leq 0.05$ ) was present only in the 2000 mg tetryl dose group (females).

5. Platelets:

There were no significant changes in total platelets in any treatment group.

6. Heinz Bodies:

There were no significant changes in heinz bodies in any treatment group.

7. Reticulocytes:

A significant increase ( $p \leq 0.05$ ) was noted only in the 2500 and 2000 mg tetryl dose groups (females).

8. Methemoglobin:

A significant increase ( $p \leq 0.05$ ) was present in females receiving 5000 mg diet and in males receiving 5000, 2500 and 2000 mg tetryl diet.

### Clinical Chemistry

The mean group values for each analyte are compiled in Tables 10 (females) and 11 (males). Individual data are present in Appendix E.

1. Total Protein:

The mean values for females ranged from 5.5 to 6.2 g/dl while in males the range was 5.8 to 6.5. Significant increases ( $p \leq 0.05$ ) occurred in all the groups except the 500 mg tetryl dose group (females).

2. Albumin:

The mean values for females ranged from 4.0 to 4.5 g/dl while in males the range was 4.2 to 4.7. There were significant increases ( $p \leq 0.05$ ) in all groups except the 500 mg tetryl dose group (females).

3. Calcium:

The mean values for females ranged from 10.4 to 10.9 mg/dl while in males the range was 10.7 to 11.8. Significant increases ( $p \leq 0.05$ ) were evident in the 1250 and 500 mg male tetryl dose groups but not in any female groups.

4. Total Bilirubin:

The mean values for females ranged from 0.08 to 0.30 mg/dl while in males the range was 0.08 to 0.16. Females receiving 5000, 2500 and 2000 mg tetryl diet had significant increased ( $p \leq 0.05$ ) values. No changes were evident in males.

5. Blood Urea Nitrogen (BUN):

The mean values for females ranged from 18.0 to 22.2 mg/dl while in males the range was 18.4 to 19.4. There were no significant differences amongst the groups.

6. Creatinine:

The mean values for females ranged from 0.52 to 0.60 mg/dl while in males the range was 0.54 to 0.62. There were no significant differences amongst the groups.

7. Aspartate Aminotransferase (AST):

The mean values for females ranged from 132 to 162 IU/L while in males the range was 132 to 232. There were no significant differences amongst the groups.

8. Alanine Aminotransferase (ALT):

The mean values for females ranged from 47 to 62 IU/L while in males the range was 57 to 106. There were no significant differences amongst the groups.

9. Alkaline Phosphatase (ALK Phos):

The mean values for females ranged from 95 to 124 IU/L while in males the range was 111 to 157. All male groups except the 500 mg tetryl group, had significantly lower values ( $p \leq 0.05$ ) while females demonstrated no significant changes.

10. Sodium:

The mean values for females ranged from 141 to 143 mmol/L while in males the range was 142 to 143. There were no significant differences amongst the groups except for a minimal decrease in the high dose female group.

11. Potassium:

The mean values for females ranged from 4.4 to 4.8 mmol/L while in males the range was 5.0 to 5.3. There were no significant changes amongst the groups.

12. Glucose:

The mean values for females ranged from 113 to 127 mg/dl while in males the range was 134 to 178. Only one group (2500 mg tetryl; males) displayed a significant increase ( $p \leq 0.05$ ).

13. Phosphorus:

The mean values for females ranged from 9.1 to 9.5 mg/dl while in males the range was 10.4 to 11.4. There were no significant changes amongst the groups.

Clinical Observations

Clinical observations are listed in Appendix F. There were no clinical observations that were meaningful.

Mortality

There were no early deaths in any of the groups.

Gross Pathology

Gross changes noted at the terminal sacrifice were not remarkable.

Histopathology (Appendix G)

All tissues were histopathologically examined in control and high dose animals of both sexes while the kidneys were reviewed in all male groups. The only change that was considered treatment related was a dose related increase of tubular hyaline droplets in the kidneys at all dose levels of males. All other diagnoses as listed in the tables should be considered spontaneous since their incidence and severity levels were low.

### SUMMARY

The administration to Fischer 344 rats of N-Methyl-N, 2,4,6-Tetranitroaniline at various doses in the diet for fourteen days resulted in the following significant findings:

1. A significant decrease in final body weight was noted in males receiving 5000 mg tetryl.
2. Relative organs weights were significantly altered in the 5000 mg tetryl dose group involving the liver (females), kidneys (males) and spleen (females). The 2500 mg tetryl dose group displayed a marked relative weight change of the liver only (females).
3. Hematology data indicated significant increased values relating to reticulocytes (females) and methemoglobin (females and males) in high (5000 mg tetryl) and mid dose (2000 and 2500 mg tetryl) groups.
4. Total protein and albumin were significantly increased in all groups except females receiving 50 mg tetryl while alkaline phosphatase was decreased in the same female groups.
5. Increased hyaline droplet deposition in the renal cortical epithelium was evident in all male treatment groups.

## REFERENCES

Burlinson, N.E. (1980) Fate of TNT in an Aquatic Environment: Photodecomposition vs. Biotransformation. Final report. Silver Spring, Maryland: Naval Weapons Center, NSWC/TR-79-445.

Fitzgerald, G.B., Austin, A., Desai, L.S. and Reddy, G. (1992a). Acute Toxicological Evaluation of N-methyl-N,2,4,6-tetranitroaniline. J. Amer. Coll. Toxicol. Acute Toxicity Data: Part B. 1, 167-168.

Fitzgerald, G.B., DiGiulio, N., Desai, L.S. and Reddy, G. (1992b). Acute Toxicological Evaluation of 1,3-Dinitrobenzene. J. Amer. Coll. Toxicol. Acute Toxicity Data: Part B. 1, 168-169.

Lee, R.G., Bithell, T.C., and Foerster, J. (1993). Wintrobe's Clinical Hematology, p.1048.

Fitzgerald, G.B., DiGiulio, N., Desai, L.S. and Reddy, G. (1992c). Acute Toxicological Evaluation of 1,3,5-Trinitrobenzene. J. Amer. Coll. Toxicol. Acute Toxicity Data: Part B. 1, 169-170.

McGregor, D.B., Riach, C.G., Hastwell, R.M. and Dacre, J.C. (1980). Genotoxic Activity in Microorganisms of Tetryl, 1,3-Dinitrobenzene and 1,3,5-Trinitrobenzene. Environ. Mut. 2, 531-541.

Reddy, T.V., Wan, L., Lin, E.L.C., Daniel, F.B. and Reddy, G. (1991). Formation and Persistence of 1,3,5-Trinitrobenzene Adducts with Blood Proteins and Tissue DNA. Toxicologist, 11, 131.

U.S. EPA. (1990). Health and Environmental Effects Document for Trinitrophenylmethylnitramine. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. ECAO-CIN-GO91.

Von Burg, R. (1989). Toxicology Update: Dinitrobenzene. J. Appl. Toxicol. 9, 199-202.

Walsh, M.E. and Jenkins, T.F. (1992). Identification of TNT Transformation Products in Soil. U.S. Army Corps of Engineers, Cold Regions Research and Engineering Laboratory, Special Report 92-16.

# TABLES

Table 1: Food and Water Consumption

Dose Groups (mg tetra/kg diet)	Food (g/kg b.w./day)	Water
Females		
0	76.23±1.43	108.90±2.89
5000	70.25±4.36	114.60±7.35
2500	69.11±1.30	135.21±11.96
2000	67.86±2.73	121.22±3.09
1250	70.13±0.86	116.23±2.87
500	75.49±1.83	130.16±3.75
Males		
0	76.25±0.87	97.44±1.86
5000	73.96±2.89	98.82±3.16
2500	72.87±2.74	96.73±3.15
2000	72.77±1.39	97.47±4.16
1250	73.05±0.46	103.30±2.12
500	75.09±0.71	98.70±1.61

Mean ± Standard Error.

Table 2: Daily Consumption of Tetryl

Dose Groups (mg tetryl/kg diet)	Calculated Dose (mg tetryl/kg b.w.)	
	Females	Males
0		
5000	374.42 ± 30.62	349.76 ± 38.56
2500	178.98 ± 13.33	170.57 ± 6.71
2000	130.3 ± 5.96	121.01 ± 10.05
1250	82.57 ± 1.30	80.07 ± 1.98
500	32.11 ± 0.90	31.86 ± 1.79

Mean ± Standard Error.

Table 3: Body Weights (grams)

Dose Groups (mg tetra/kg diet)	Week 1	Week 2	Necropsy**
Females			
0	150.03±1.36	152.84±1.73	146.21±3.00
5000	150.21±2.89	147.94±3.11	141.47±3.16
2500	148.77±2.61	149.96±2.36	142.15±2.54
2000	149.14±1.47	149.38±2.12	141.70±2.21
1250	151.72±1.71	155.36±1.90	147.64±2.28
500	150.45±2.65	153.36±2.46	146.59±2.93
Males			
0	213.90±2.15	233.70±2.41	219.43±3.36
5000	205.39±4.60	204.72±4.25 *	198.65±3.37 *
2500	211.11±3.82	215.54±4.70	213.61±4.01
2000	212.04±5.00	218.52±4.65	217.16±7.16
1250	213.59±2.57	222.72±3.14	221.52±3.60
500	215.03±2.17	225.86±2.87	224.86±3.77

Mean ± Standard Error

\* Significantly different from the control group ( $p \leq .05$ ) by the Dunnett's test.

\*\* All rats fasted for 16-18 hours.

Table 4: Organ Weights (grams)/Females

	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
Liver	4.31±0.22	5.02±0.23	4.93±0.34	4.57±0.08	4.65±0.09	4.58±0.11
Kidneys	1.08±0.02	1.16±0.05	1.11±0.06	1.09±0.03	1.15±0.03	1.10±0.02
Heart	0.57±0.02	0.62±0.06	0.58±0.02	0.57±0.02	0.58±0.02	0.58±0.02
Ovaries	0.11±0.00	0.11±0.02	0.12±0.01	0.12±0.01	0.12±0.01	0.13±0.01
Brain	1.69±0.02	1.64±0.03	1.71±0.02	1.64±0.03	1.64±0.04	1.57±0.07
Spleen	0.42±0.01	0.45±0.02	0.41±0.02	0.43±0.01	0.42±0.01	0.43±0.02
Adrenals	0.06±0.00	0.06±0.00	0.07±0.00	0.06±0.00	0.06±0.00	0.07±0.00
Lungs	0.83±0.02	0.90±0.05	0.89±0.06	0.78±0.05	0.85±0.04	0.84±0.04
Thymus	0.27±0.01	0.28±0.02	0.27±0.01	0.27±0.01	0.29±0.01	0.29±0.02

Mean ± Standard Error

Table 5: Organ Weights (grams)/Males

	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
Liver	6.83±0.15	7.65±0.28	7.07±1.03	7.97±0.42	7.86±0.23	7.70±0.29
Kidneys	1.70±0.03	1.73±0.08	1.82±0.06	1.79±0.07	1.79±0.02	1.83±0.10
Heart	0.76±0.01	0.73±0.04	0.78±0.04	0.77±0.04	0.75±0.04	0.74±0.01
Testes	3.90±0.14	3.48±0.16	3.88±0.12	3.89±0.17	3.78±0.14	3.84±0.21
Brain	1.73±0.06	1.72±0.02	1.74±0.05	1.71±0.07	1.77±0.02	1.81±0.04
Spleen	0.47±0.05	0.47±0.01	0.51±0.01	0.50±0.02	0.50±0.01	0.50±0.01
Adrenals	0.05±0.01	0.06±0.00	0.07±0.00	0.17±0.10	0.06±0.00	0.07±0.01
Lungs	1.01±0.04	0.91±0.04	1.10±0.03	1.09±0.03	1.10±0.06	1.09±0.03
Thymus	0.32±0.01	0.31±0.02	0.29±0.01	0.28±0.03	0.28±0.03	0.29±0.03

Mean ± Standard Error

Table 6: Organ-to-Body Weight Ratios/Females

	Dose Groups (mg tetry/kg diet)					
(%)	0	5000	2500	2000	1250	500
Liver	2.94±0.12	3.55±0.13 *	3.46±0.18 *	3.22±0.06	3.15±0.06	3.12±0.03
Kidneys	0.74±0.02	0.82±0.03	0.79±0.03	0.77±0.02	0.78±0.01	0.75±0.02
Heart	0.39±0.02	0.44±0.05	0.41±0.01	0.41±0.02	0.39±0.02	0.39±0.01
Ovaries	0.08±0.00	0.08±0.01	0.08±0.01	0.09±0.01	0.08±0.01	0.09±0.01
Brain	1.16±0.02	1.16±0.02	1.20±0.03	1.16±0.02	1.11±0.04	1.07±0.05
Spleen	0.28±0.01	0.32±0.01 *	0.29±0.01	0.30±0.01	0.28±0.01	0.29±0.01
Adrenals	0.04±0.00	0.04±0.00	0.05±0.00	0.04±0.00	0.04±0.00	0.04±0.00
Lungs	0.57±0.01	0.64±0.04	0.62±0.03	0.55±0.03	0.58±0.04	0.57±0.03
Thymus	0.18±0.01	0.20±0.01	0.19±0.01	0.19±0.01	0.20±0.01	0.20±0.01

Mean ± Standard Error

\* Significantly different from the control group ( $p \leq .05$ ) by the Dunnett's test.

Table 7: Organ-to-Body Weight Ratios/Males

(%)	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
Liver	3.11±0.04	3.85±0.12	3.31±0.47	3.66±0.09	3.55±0.05	3.42±0.09
Kidneys	0.77±0.02	0.87±0.03 *	0.85±0.02	0.82±0.01	0.81±0.01	0.81±0.03
Heart	0.34±0.00	0.37±0.01	0.37±0.01	0.36±0.01	0.34±0.02	0.33±0.01
Testes	1.78±0.05	1.75±0.04	1.82±0.08	1.80±0.11	1.71±0.06	1.71±0.11
Brain	0.79±0.02	0.86±0.02	0.81±0.01	0.79±0.04	0.80±0.01	0.81±0.02
Spleen	0.21±0.02	0.24±0.00	0.24±0.01	0.23±0.01	0.23±0.00	0.22±0.00
Adrenals	0.02±0.00	0.03±0.00	0.03±0.00	0.07±0.04	0.03±0.00	0.03±0.00
Lungs	0.46±0.02	0.46±0.01	0.51±0.02	0.50±0.01	0.50±0.03	0.49±0.01
Thymus	0.15±0.01	0.16±0.01	0.13±0.00	0.13±0.01	0.12±0.01	0.13±0.01

Mean ± Standard Error

\* Significantly different from the control group ( $p \leq .05$ ) by the Dunnett's test.

Table 8: Hematology Values/Females

	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
RBC (x10 <sup>6</sup> /μl)	8.50 ±0.25	8.19 ±0.35	8.45 ±0.30	8.05 ±0.36	8.40 ±0.15	8.50 ±0.26
Hemoglobin (g/dL)	15.84 ±0.34	14.76 * ±0.48	15.46 ±0.51	14.68 * ±0.66	15.44 ±0.17	15.80 ±0.64
Hematocrit (%)	45.42 ±0.98	43.48 ±1.29	44.90 ±1.12	42.74 * ±2.07	44.68 ±0.73	45.78 ±1.41
WBC (x10 <sup>3</sup> /μL)	4.30 ±0.68	5.06 ±0.61	4.46 ±0.40	3.86 ±0.81	4.08 ±0.45	4.94 ±0.65
Platelets (x10 <sup>3</sup> /μL)	701.00 ±60.49	722.00 ±113.07	723.20 ±88.35	734.60 ±80.18	720.00 ±13.49	719.60 ±103.87
Segmented Leukocytes (%)	16.04 ±2.95	15.98 ±4.24	14.96 ±1.56	17.98 ±1.91	18.86 ±3.70	16.26 ±1.58
Lymphocytes (%)	80.14 ±2.96	79.84 ±4.60	81.44 ±1.33	78.30 ±1.66	76.78 ±3.71	80.16 ±1.46
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
Monocytes (%)	1.08 ±0.24	1.22 ±0.25	1.08 ±0.19	1.32 ±0.61	1.44 ±0.39	1.10 ±0.20
Eosinophils (%)	1.70 ±0.82	1.76 ±0.47	1.56 ±0.56	1.12 ±1.01	1.92 ±0.41	1.50 ±0.55
Reticulocytes (%)	1.78 ±0.18	2.22 ±0.15	2.46 * ±0.42	2.30 * ±0.31	2.08 ±0.24	1.98 ±0.38
MetHb (%)	0.58 ±0.37	2.18 * ±0.50	1.28 ±0.63	0.98 ±0.75	0.84 ±0.62	0.62 ±0.39

Mean ± Standard Deviation

\* Significantly different from the control group (p ≤ 0.05) by the Dunnett's test.

Table 9: Hematology Values/Males

	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
RBC ( $\times 10^6/\mu\text{L}$ )	9.07 $\pm 0.16$	9.06 $\pm 0.29$	9.15 $\pm 0.18$	9.08 $\pm 0.17$	9.19 $\pm 0.17$	9.01 $\pm 0.22$
Hemoglobin (g/dL)	16.20 $\pm 0.43$	15.62 $\pm 0.48$	15.92 $\pm 0.19$	15.88 $\pm 0.50$	16.12 $\pm 0.25$	16.00 $\pm 0.45$
Hematocrit (%)	48.12 $\pm 1.37$	46.82 $\pm 1.43$	47.90 $\pm 0.70$	47.76 $\pm 1.81$	48.46 $\pm 1.17$	47.78 $\pm 1.55$
WBC ( $\times 10^3/\mu\text{L}$ )	4.82 $\pm 1.03$	4.14 $\pm 1.05$	4.94 $\pm 0.73$	4.30 $\pm 0.94$	4.96 $\pm 0.71$	4.56 $\pm 0.45$
Platelets ( $\times 10^3/\mu\text{L}$ )	755.00 $\pm 40.60$	748.60 $\pm 96.66$	739.80 $\pm 94.48$	683.60 $\pm 62.29$	729.40 $\pm 64.04$	754.40 $\pm 68.01$
Segmented Leukocytes (%)	24.72 $\pm 6.61$	18.52 $\pm 5.39$	18.36 $\pm 2.20$	18.80 $\pm 2.45$	22.26 $\pm 6.99$	25.32 $\pm 5.56$
Lymphocytes (%)	71.66 $\pm 6.08$	78.44 $\pm 5.97$	77.74 $\pm 2.88$	76.82 $\pm 2.98$	73.88 $\pm 7.01$	70.74 $\pm 5.97$
Heinz Bodies (%)	0.0 $\pm 0.00$	0.0 $\pm 0.00$	0.0 $\pm 0.00$	0.0 $\pm 0.00$	0.0 $\pm 0.00$	0.0 $\pm 0.00$
Monocytes (%)	1.20 $\pm 0.33$	0.94 $\pm 0.30$	1.26 $\pm 0.15$	1.72 $\pm 1.36$	1.12 $\pm 0.36$	1.30 $\pm 0.38$
Eosinophils (%)	1.28 $\pm 0.61$	1.06 $\pm 0.35$	1.54 $\pm 0.91$	1.44 $\pm 0.53$	1.64 $\pm 1.08$	1.58 $\pm 0.59$
Reticulocytes (%)	1.78 $\pm 0.08$	1.60 $\pm 0.31$	1.90 $\pm 0.21$	1.82 $\pm 0.20$	1.80 $\pm 0.16$	1.86 $\pm 0.09$
MetHb (%)	0.46 $\pm 0.34$	2.22* $\pm 0.86$	1.78* $\pm 1.38$	1.64* $\pm 0.45$	0.90 $\pm 0.40$	0.60 $\pm 0.35$

Mean  $\pm$  Standard Deviation\* Significantly different from the control group ( $p \leq 0.05$ ) by the Dunnett's test.

Table 10: Clinical Chemistry Measurements/Females

	Dose Groups (mg tetryl/kg diet)					
	0	5000	2500	2000	1250	500
Total Protein (g/dl)	5.54 ±0.11	6.12* ±0.30	6.20* ±0.21	6.04* ±0.48	6.00* ±0.10	5.80 ±0.16
Albumin (g/dl)	4.00 ±0.16	4.46* ±0.11	4.54* ±0.13	4.38* ±0.26	4.34* ±0.13	4.20 ±0.10
Calcium (mg/dl)	10.46 ±0.23	10.90 ±0.14	10.60 ±0.36	10.58 ±0.36	10.68 ±0.23	10.42 ±0.33
Phosphorus (mg/dl)	9.12 ±0.80	9.12 ±0.67	9.34 ±0.44	9.34 ±0.80	9.18 ±0.61	9.46 ±0.80
Total Bilirubin (mg/dl)	0.08 ±0.04	0.30* ±0.07	0.18* ±0.04	0.18* ±0.04	0.14 ±0.05	0.10 ±0.00
BUN (mg/dl)	19.4 ±2.07	22.20 ±3.42	18.00 ±1.58	18.20 ±1.30	19.80 ±3.11	19.20 ±1.79
Creatinine (mg/dl)	0.54 ±0.05	0.60 ±0.00	0.58 ±0.04	0.58 ±0.04	0.56 ±0.05	0.52 ±0.04
AST (U/L)	131.80 ±18.50	161.60 ±17.31	154.40 ±65.99	132.80 ±31.08	134.80 ±24.28	134.80 ±34.39
ALT (U/L)	59.20 ±17.81	46.60 ±6.54	61.80 ±37.78	53.20 ±19.43	47.00 ±4.06	58.20 ±19.49
ALK Phos. (U/L)	111.80 ±22.97	124.00 ±25.29	95.20 ±11.82	97.00 ±12.02	99.20 ±9.34	106.40 ±12.42
Glucose (mg/dl)	125.00 ±26.03	127.20 ±8.17	120.40 ±14.52	127.20 ±16.39	113.40 ±12.03	127.40 ±13.61
Sodium (mmol/L)	142.60 ±1.82	140.80* ±0.45	142.00 ±0.71	142.00 ±0.71	141.60 ±0.89	143.40 ±0.55
Potassium (mmol/L)	4.36 ±0.26	4.76 ±0.26	4.52 ±0.24	4.50 ±0.37	4.44 ±0.26	4.40 ±0.45

Mean ± Standard Deviation

\* Significantly different from the control group ( $p \leq 0.05$ ) by the Dunnett's test.

Table 11: Clinical Chemistry Measurements/Males

	Dose Groups (mg tetra/kg diet)					
	0	5000	2500	2000	1250	500
Total Protein (g/dl)	5.82 ±0.08	6.46* ±0.21	6.48* ±0.13	6.48* ±0.26	6.42* ±0.15	6.36* ±0.19
Albumin (g/dl)	4.18 ±0.13	4.66* ±0.15	4.58* ±0.08	4.60* ±0.10	4.54* ±0.09	4.54* ±0.21
Calcium (mg/dl)	10.67 ±0.10	11.80 ±0.24	11.14 ±0.25	11.10 ±0.47	11.22* ±0.16	11.20* ±0.29
Phosphorus (mg/dl)	11.25 ±0.19	10.36 ±1.05	10.68 ±0.50	11.36 ±1.05	10.94 ±0.72	11.44 ±0.47
Total Bilirubin (mg/dl)	0.08 ±0.05	0.16 ±0.05	0.12 ±0.04	0.14 ±0.05	0.10 ±0.00	0.10 ±0.07
BUN (mg/dl)	18.40 ±3.44	19.00 ±1.87	18.60 ±1.67	19.40 ±0.89	19.20 ±0.84	19.20 ±2.77
Creatinine (mg/dl)	0.54 ±0.09	0.56 ±0.05	0.60 ±0.00	0.58 ±0.08	0.60 ±0.00	0.62 ±0.04
AST (U/L)	158.50 ±30.95	144.60 ±59.33	132.20 ±24.70	231.60 ±219.25	163.80 ±128.71	154.20 ±22.71
ALT (U/L)	78.00 ±22.99	56.60 ±22.57	57.00 ±9.17	106.20 ±120.15	69.60 ±62.32	62.20 ±9.20
ALK Phos. (U/L)	157.00 ±7.97	110.80* ±12.28	121.60* ±5.41	129.20* ±7.85	134.00* ±16.63	155.00 ±16.99
Glucose (mg/dl)	133.60 ±16.86	157.80 ±16.69	178.40* ±7.50	164.80 ±31.04	164.20 ±22.22	156.80 ±15.35
Sodium (mmol/L)	142.00 ±2.12	142.20 ±0.84	143.00 ±0.71	142.40 ±0.89	142.60 ±0.89	142.00 ±0.71
Potassium (mmol/L)	5.12 ±0.37	5.06 ±0.43	5.26 ±0.38	5.28 ±0.67	4.96 ±0.65	5.32 ±0.72

Mean ± Standard Deviation

\* Significantly different from the control group ( $p \leq 0.05$ ) by the Dunnett's test.

APPENDIX A

FOOD AND WATER  
CONSUMPTION

Individual Food and Water Consumption/Females

Dose Groups (mg tetryl/kg diet)	Animal Number	Food (g/wk)		Water (g/wk)	
		Week 1	Week 2	Week 1	Week 2
0	1	72.7	91.8	108.2	125.7
	2	69.2	73.2	91.4	106.1
	3	70.1	80.3	105.4	124.0
	4	65.7	74.1	89.2	106.8
	5	72.5	77.8	101.1	114.1
5000	6	39.7 **	62.0	119.6	148.1
	7	18.8 **	68.9	91.8	120.2
	8	21.8 **	91.7	109.3	152.7
	9	35.8 **	74.0	93.6	121.2
	10	56.2	81.1	78.1	95.9
2500	11	58.2	80.4	93.1	124.0
	12	63.0	81.9	143.7	197.5
	13	41.8	76.6	110.3	131.1
	14	53.5	77.1	118.7	164.7
	15	54.4	72.9	104.9	131.6
2000	16	64.2	73.5	98.9	133.2
	17	62.7	75.2	105.0	126.7
	18	65.0	79.5	110.9	146.8
	19	60.7	73.7	112.3	133.8
	20	50.5	57.1	103.2	122.4

\*Excessive Spillage

\*\*Partial week measurement due to excessive spillage

Week 1 is only 6 days.

# Individual Food and Water Consumption/Females

Dose Groups (mg tetra/kg diet)	Animal Number	Food (g/wk)		Water (g/wk)	
		Week 1	Week 2	Week 1	Week 2
1250	21	61.4	74.7	106.6	137.3
	22	63.8	77.3	102.4	132.1
	23	70.1	81.7	117.0	138.5
	24	64.8	79.7	101.2	117.8
	25	63.3	66.7	99.4	116.0
500	26	66.2	78.7	131.2	155.9
	27	68.3	77.9	128.0	144.1
	28	71.1	85.8	108.9	132.8
	29	67.1	75.3	125.8	141.3
	30	68.5	82.5	101.6	125.1

\*Excessive Spillage

Week 1 is only 6 days.

Individual Food and Water Consumption/Males

Dose Groups (mg tetra/kg diet)	Animal Number	Food (g/wk)		Water (g/wk)	
		Week 1	Week 2	Week 1	Week 2
0	31	102.5	116.3	126.4	150.8
	32	109.5	119.6	136.5	165.4
	33	103.7	108.5	129.8	148.7
	34	103.1	113.4	124.4	150.1
	35	96.7	106.6	117.8	140.0
5000	36	28.4	113.3	121.1	166.9
	37	*	60.0 **	116.4	167.2
	38	81.7	65.9 **	105.8	150.5
	39	57.8 **	80.5 **	107.3	142.2
	40	76.9	97.7	117.5	156.0
2500	41	96.9	115.3	137.1	169.4
	42	86.2	106.8	115.6	137.8
	43	85.8	108.4	112.2	133.9
	44	90.5	104.7	123.8	148.7
	45	32.0 **	70.3 **	120.6	159.0
2000	46	90.8	117.4	126.0	158.7
	47	95.7	105.6	148.5	177.2
	48	103.7	112.7	120.6	145.7
	49	97.1	110.7	115.5	136.3
	50	85.7	100.1	111.5	136.9

\*Excessive Spillage

\*\*Partial week measurement due to excessive spillage

Week 1 is only 6 days.

# Individual Food and Water Consumption/Males

Dose Groups (mg tetra/kg diet)	Animal Number	Food (g/wk)		Water (g/wk)	
		Week 1	Week 2	Week 1	Week 2
1250	51	97.8	119.9	145.5	119.6
	52	97.7	112.3	143.0	176.2
	53	97.7	114.7	134.8	157.5
	54	94.1	104.8	126.4	158.6
	55	93.9	107.4	121.8	145.0
500	56	101.5	114.4	132.3	150.0
	57	102.8	121.6	144.8	165.7
	58	105.2	115.7	133.1	146.5
	59	96.2	117.3	128.2	146.8
	60	95.2	105.4	123.1	148.2

\*Excessive Spillage

Week 1 is only 6 days.

APPENDIX B  
BODY WEIGHTS

# INDIVIDUAL BODY WEIGHTS (GRAMS)

GP-ANI NUMBER		WEEK 1	WEEK 2	TERMINAL WEIGHT
1	01	152.00	155.70	154.02
1	02	146.20	148.60	141.99
1	03	148.70	155.70	148.05
1	04	145.60	148.60	137.06
1	05	150.60	155.60	149.95
2	06	159.80	158.80	152.66
2	07	154.80	149.20	141.12
2	08	151.90	147.40	142.67
2	09	144.30	143.90	136.11
2	10	145.90	140.40	134.79
3	11	154.80	155.40	148.74
3	12	154.90	155.90	147.71
3	13	144.30	147.30	139.55
3	14	142.80	144.70	138.35
3	15	144.10	146.50	136.39
4	16	150.30	153.20	145.07
4	17	150.00	154.00	145.83
4	18	152.10	151.00	143.45
4	19	147.90	145.10	140.52
4	20	144.80	143.60	133.65
5	21	148.40	154.00	146.30
5	22	151.50	155.30	151.84
5	23	155.40	162.00	151.19
5	24	148.30	155.30	149.52
5	25	145.90	150.20	139.37
6	26	155.60	160.80	156.12
6	27	152.10	154.00	145.80
6	28	150.50	153.80	148.86
6	29	147.60	152.90	143.73
6	30	139.20	145.30	138.43

# INDIVIDUAL BODY WEIGHTS (GRAMS)

GP-ANI NUMBER		WEEK 1	WEEK 2	TERMINAL WEIGHT
7	31	211.90	227.60	227.72
7	32	214.80	230.40	226.42
7	33	206.40	218.60	212.14
7	34	208.80	223.70	218.89
7	35	203.10	218.20	212.00
8	36	214.00	215.50	210.00
8	37	211.70	208.30	198.21
8	38	211.80	207.40	205.81
8	39	203.20	202.50	194.05
8	40	187.90	189.90	185.19
9	41	220.10	230.60	226.82
9	42	210.40	217.40	215.22
9	43	206.60	210.30	209.82
9	44	208.40	217.30	213.95
9	45	199.00	202.10	202.24
10	46	226.00	232.30	240.52
10	47	209.90	219.20	215.27
10	48	208.30	221.70	219.91
10	49	206.50	215.90	214.43
10	50	193.30	203.50	195.67
11	51	215.10	232.10	233.97
11	52	212.40	226.10	223.42
11	53	210.20	223.70	220.21
11	54	203.50	216.80	217.65
11	55	203.90	214.90	212.37
12	56	212.00	228.40	234.51
12	57	214.40	233.00	231.61
12	58	209.40	228.00	224.92
12	59	208.90	224.00	218.89
12	60	203.40	215.90	214.39

APPENDIX C  
ORGAN WEIGHTS

# INDIVIDUAL ORGAN WEIGHTS (grams)

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
1 01	154.02	1.062	0.885	4.462	0.690	0.575	2.897
1 02	141.99	1.097	0.788	4.127	0.773	0.555	2.907
1 03	148.05	1.149	0.832	4.981	0.776	0.562	3.364
1 04	137.06	1.001	0.780	3.633	0.730	0.569	2.651
1 05	149.95	1.086	0.878	4.334	0.724	0.586	2.890
2 06	152.66	1.340	0.990	5.505	0.878	0.648	3.606
2 07	141.12	1.201	0.907	5.664	0.851	0.643	4.014
2 08	142.67	1.002	0.758	4.720	0.702	0.531	3.308
2 09	136.11	1.123	0.807	4.563	0.825	0.593	3.352
2 10	134.79	1.149	1.049	4.661	0.852	0.778	3.458
3 11	148.74	1.333	1.060	5.441	0.896	0.713	3.658
3 12	147.71	1.017	0.928	5.949	0.689	0.628	4.027
3 13	139.55	1.112	0.949	4.352	0.797	0.680	3.119
3 14	138.35	1.108	0.740	4.737	0.801	0.535	3.424
3 15	136.39	1.022	0.766	4.159	0.749	0.562	3.049
4 16	145.07	1.141	0.966	4.523	0.787	0.666	3.118
4 17	145.83	0.981	0.796	4.506	0.673	0.546	3.090
4 18	143.45	1.113	0.748	4.880	0.776	0.521	3.402
4 19	140.52	1.126	0.696	4.462	0.801	0.495	3.175
4 20	133.65	1.068	0.683	4.463	0.799	0.511	3.339
5 21	146.30	1.100	0.893	4.555	0.752	0.610	3.113
5 22	151.84	1.199	0.749	4.482	0.790	0.493	2.952
5 23	151.19	1.225	0.813	4.977	0.810	0.538	3.292
5 24	149.52	1.158	0.796	4.729	0.774	0.532	3.163
5 25	139.37	1.067	0.982	4.501	0.766	0.705	3.230
6 26	156.12	1.130	0.897	4.873	0.724	0.575	3.121
6 27	145.80	1.073	0.796	4.605	0.736	0.546	3.158
6 28	148.86	1.144	0.896	4.752	0.769	0.602	3.192
6 29	143.73	1.053	0.687	4.299	0.733	0.478	2.991
6 30	138.43	1.119	0.927	4.357	0.808	0.670	3.147

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
1	01	154.02	0.548	1.775	0.426	0.356	1.152	0.277
1	02	141.99	0.572	1.629	0.417	0.403	1.147	0.294
1	03	148.05	0.516	1.685	0.400	0.349	1.138	0.270
1	04	137.06	0.623	1.685	0.407	0.455	1.229	0.297
1	05	149.95	0.613	1.694	0.430	0.409	1.130	0.287
2	06	152.66	0.552	1.737	0.464	0.362	1.138	0.304
2	07	141.12	0.529	1.602	0.508	0.375	1.135	0.360
2	08	142.67	0.668	1.599	0.470	0.468	1.121	0.329
2	09	136.11	0.822	1.633	0.423	0.604	1.200	0.311
2	10	134.79	0.509	1.644	0.405	0.378	1.220	0.300
3	11	148.74	0.617	1.639	0.478	0.415	1.102	0.321
3	12	147.71	0.593	1.741	0.441	0.401	1.179	0.299
3	13	139.55	0.565	1.702	0.388	0.405	1.220	0.278
3	14	138.35	0.521	1.763	0.390	0.377	1.274	0.282
3	15	136.39	0.610	1.686	0.375	0.447	1.236	0.275
4	16	145.07	0.588	1.723	0.441	0.405	1.188	0.304
4	17	145.83	0.615	1.651	0.445	0.422	1.132	0.305
4	18	143.45	0.572	1.619	0.456	0.399	1.129	0.318
4	19	140.52	0.480	1.569	0.393	0.342	1.117	0.280
4	20	133.65	0.614	1.645	0.414	0.459	1.231	0.310
5	21	146.30	0.550	1.690	0.412	0.376	1.155	0.282
5	22	151.84	0.534	1.462	0.412	0.352	0.963	0.271
5	23	151.19	0.658	1.692	0.463	0.435	1.119	0.306
5	24	149.52	0.529	1.681	0.390	0.354	1.124	0.261
5	25	139.37	0.605	1.673	0.414	0.434	1.200	0.297
6	26	156.12	0.619	1.595	0.506	0.396	1.022	0.324
6	27	145.80	0.629	1.643	0.424	0.431	1.127	0.291
6	28	148.86	0.578	1.698	0.395	0.388	1.141	0.265
6	29	143.73	0.506	1.308	0.381	0.352	0.910	0.265
6	30	138.43	0.553	1.624	0.424	0.399	1.173	0.306

GP-ANI NUMBER		BODY WEIGHT	ADRENALS WEIGHT	THYMUS WEIGHT	OVARIES WEIGHT	% ADRENALS	% THYMUS	% OVARIES
1	01	154.02	0.063	0.242	0.115	0.041	0.157	0.075
1	02	141.99	0.073	0.254	0.125	0.051	0.179	0.088
1	03	148.05	0.056	0.269	0.101	0.038	0.182	0.066
1	04	137.06	0.058	0.304	0.115	0.042	0.222	0.084
1	05	149.95	0.058	0.261	0.106	0.039	0.174	0.071
2	06	152.66	0.068	0.260	0.149	0.045	0.170	0.098
2	07	141.12	0.070	0.348	0.165	0.050	0.247	0.117
2	08	142.67	0.061	0.244	0.085	0.043	0.171	0.060
2	09	136.11	0.045	0.254	0.086	0.033	0.187	0.063
2	10	134.79	0.054	0.283	0.064	0.040	0.210	0.047
3	11	148.74	0.067	0.296	0.143	0.045	0.199	0.096
3	12	147.71	0.073	0.286	0.107	0.049	0.194	0.072
3	13	139.55	0.060	0.250	0.082	0.043	0.179	0.059
3	14	138.35	0.072	0.222	0.136	0.052	0.160	0.098
3	15	136.39	0.072	0.282	0.115	0.053	0.207	0.084
4	16	145.07	0.070	0.287	0.129	0.048	0.198	0.089
4	17	145.83	0.073	0.253	0.161	0.050	0.173	0.110
4	18	142.45	0.051	0.254	0.114	0.036	0.177	0.079
4	19	140.52	0.050	0.287	0.097	0.036	0.204	0.069
4	20	133.65	0.057	0.264	0.112	0.043	0.198	0.084
5	21	146.30	0.051	0.241	0.076	0.035	0.165	0.052
5	22	151.84	0.057	0.299	0.165	0.038	0.197	0.109
5	23	151.19	0.067	0.306	0.121	0.044	0.202	0.080
5	24	149.52	0.050	0.286	0.115	0.033	0.191	0.077
5	25	139.37	0.063	0.317	0.100	0.045	0.227	0.072
6	26	156.12	0.061	0.352	0.158	0.039	0.225	0.101
6	27	145.80	0.065	0.278	0.106	0.045	0.191	0.073
6	28	148.86	0.070	0.262	0.094	0.047	0.176	0.063
6	29	143.73	0.056	0.247	0.110	0.039	0.172	0.077
6	30	138.43	0.074	0.298	0.164	0.053	0.215	0.118

GP-ANI NUMBER		BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
7	31	227.72	1.652	1.133	7.193	0.725	0.498	3.159
7	32	226.42	1.708	0.958	7.034	0.754	0.423	3.107
7	33	212.14	1.652	1.008	6.910	0.779	0.475	3.257
7	34	218.89	1.813	1.077	6.670	0.828	0.492	3.047
7	35	212.00	1.669	0.878	6.361	0.787	0.414	3.000
8	36	210.00	1.935	1.010	8.204	0.921	0.481	3.907
8	37	198.21	1.618	0.865	6.900	0.816	0.436	3.481
8	38	205.81	1.912	0.987	8.276	0.929	0.480	4.021
8	39	194.05	1.538	0.903	7.149	0.793	0.465	3.684
8	40	185.19	1.642	0.783	7.274	0.887	0.423	3.928
9	41	226.82	2.005	1.084	8.855	0.884	0.478	3.904
9	42	215.22	1.895	1.085	8.190	0.880	0.504	3.805
9	43	209.82	1.790	1.209	7.508	0.853	0.576	3.578
9	44	213.95	1.641	1.017	3.075	0.767	0.475	1.437
9	45	202.24	1.748	1.087	7.732	0.864	0.537	3.823
10	46	240.52	2.037	1.211	9.180	0.847	0.503	3.817
10	47	215.27	1.696	1.122	7.502	0.788	0.521	3.485
10	48	219.91	1.794	1.018	8.608	0.816	0.463	3.914
10	49	214.43	1.764	1.077	7.753	0.823	0.502	3.616
10	50	195.67	1.657	1.035	6.791	0.847	0.529	3.471
11	51	233.97	1.805	1.157	8.708	0.771	0.495	3.722
11	52	223.42	1.725	0.985	7.852	0.772	0.441	3.514
11	53	220.21	1.812	1.054	7.756	0.823	0.479	3.522
11	54	217.65	1.814	1.309	7.700	0.833	0.601	3.538
11	55	212.37	1.774	1.010	7.299	0.835	0.476	3.437
12	56	234.51	2.101	1.161	8.686	0.896	0.495	3.704
12	57	231.61	1.973	1.169	7.753	0.852	0.505	3.347
12	58	224.92	1.787	1.018	7.526	0.795	0.453	3.346
12	59	218.89	1.782	1.108	7.688	0.814	0.506	3.512
12	60	214.39	1.526	1.017	6.860	0.712	0.474	3.200

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
7	31	227.72	0.775	1.816	0.552	0.340	0.797	0.242
7	32	226.42	0.784	1.872	0.500	0.346	0.827	0.221
7	33	212.14	0.712	1.772	0.478	0.336	0.835	0.225
7	34	218.89	0.775	1.632	0.521	0.354	0.746	0.238
7	35	212.00	0.730	1.533	0.283	0.344	0.723	0.133
8	36	210.00	0.836	1.789	0.506	0.398	0.852	0.241
8	37	198.21	0.785	1.717	0.457	0.396	0.866	0.231
8	38	205.81	0.655	1.675	0.494	0.318	0.814	0.240
8	39	194.05	0.704	1.716	0.465	0.363	0.884	0.240
8	40	185.19	0.655	1.682	0.433	0.354	0.908	0.234
9	41	226.82	0.817	1.854	0.495	0.360	0.817	0.218
9	42	215.22	0.781	1.857	0.523	0.363	0.863	0.243
9	43	209.82	0.751	1.689	0.527	0.358	0.805	0.251
9	44	213.95	0.891	1.669	0.462	0.416	0.780	0.216
9	45	202.24	0.677	1.637	0.543	0.335	0.809	0.268
10	46	240.52	0.886	1.904	0.528	0.368	0.792	0.220
10	47	215.27	0.734	1.479	0.564	0.341	0.687	0.262
10	48	219.91	0.794	1.635	0.481	0.361	0.743	0.219
10	49	214.43	0.798	1.787	0.463	0.372	0.833	0.216
10	50	195.67	0.661	1.756	0.454	0.338	0.897	0.232
11	51	233.97	0.727	1.762	0.527	0.311	0.753	0.225
11	52	223.42	0.821	1.803	0.528	0.367	0.807	0.236
11	53	220.21	0.874	1.747	0.521	0.397	0.793	0.237
11	54	217.65	0.652	1.803	0.485	0.300	0.828	0.223
11	55	212.37	0.677	1.724	0.462	0.319	0.812	0.218
12	56	234.51	0.704	1.777	0.511	0.300	0.758	0.218
12	57	231.61	0.771	1.941	0.549	0.333	0.838	0.237
12	58	224.92	0.733	1.715	0.480	0.326	0.762	0.213
12	59	218.89	0.756	1.788	0.478	0.345	0.817	0.218
12	60	214.39	0.728	1.841	0.475	0.340	0.859	0.222

GP-ANI NUMBER		BODY WEIGHT	ADRENALS WEIGHT	THYMUS WEIGHT	TESTES WEIGHT	% ADRENALS	% THYMUS	% TESTES
7	31	227.72	0.081	0.308	4.440	0.036	0.135	1.950
7	32	226.42	0.027	0.311	3.849	0.012	0.137	1.700
7	33	212.14	0.041	0.336	3.564	0.019	0.158	1.680
7	34	218.89	0.053	0.281	3.842	0.024	0.128	1.755
7	35	212.00	0.054	0.368	3.808	0.025	0.174	1.796
8	36	210.00	0.064	0.290	3.932	0.030	0.138	1.872
8	37	198.21	0.052	0.258	3.515	0.026	0.130	1.773
8	38	205.81	0.077	0.362	3.643	0.037	0.176	1.770
8	39	194.05	0.067	0.372	3.357	0.035	0.192	1.730
8	40	185.19	0.055	0.290	2.957	0.030	0.157	1.597
9	41	226.82	0.065	0.302	3.518	0.029	0.133	1.551
9	42	215.22	0.079	0.284	4.009	0.037	0.132	1.863
9	43	209.82	0.080	0.270	4.261	0.038	0.129	2.031
9	44	213.95	0.062	0.284	3.759	0.029	0.133	1.757
9	45	202.24	0.068	0.300	3.852	0.034	0.148	1.905
10	46	240.52	0.574	0.361	3.834	0.239	0.150	1.594
10	47	215.27	0.074	0.301	4.386	0.034	0.140	2.037
10	48	219.91	0.068	0.280	3.556	0.031	0.127	1.617
10	49	214.43	0.063	0.260	3.532	0.029	0.121	1.647
10	50	195.67	0.051	0.173	4.164	0.026	0.088	2.128
11	51	233.97	0.054	0.331	3.726	0.023	0.141	1.593
11	52	223.42	0.064	0.325	4.200	0.029	0.145	1.880
11	53	220.21	0.069	0.277	3.355	0.031	0.126	1.524
11	54	217.65	0.052	0.288	3.867	0.024	0.132	1.777
11	55	212.37	0.068	0.156	3.730	0.032	0.073	1.756
12	56	234.51	0.063	0.240	3.295	0.027	0.102	1.405
12	57	231.61	0.119	0.399	3.908	0.051	0.172	1.687
12	58	224.92	0.063	0.257	4.425	0.028	0.114	1.967
12	59	218.89	0.052	0.343	3.446	0.024	0.157	1.574
12	60	214.39	0.063	0.235	4.116	0.029	0.110	1.920

APPENDIX D  
HEMATOLOGY DATA

# Hematology Values/Females

		Animal Number				
	Units	1	2	3	4	5
WBC	(x10 <sup>3</sup> /μl)	4.7	3.3	4.3	4.1	5.1
RBC	(x10 <sup>6</sup> /μl)	8.40	8.39	8.36	8.94	8.40
Hemoglobin	(GM%)	15.5	15.7	15.8	16.4	15.8
Hematocrit	(%)	44.1	45.4	44.9	46.6	46.1
Platelets	(x10 <sup>3</sup> /μl)	698	717	681	788	621
Neutrophils	(%)	16.4	11.3	15.7	19.1	17.7
Lymphocytes	(%)	80.0	84.5	81.3	77.7	77.2
Monocytes	(%)	1.4	0.8	1.1	0.9	1.2
Eosinophils	(%)	0.8	2.4	1.1	1.5	2.7
Methemoglobin	(%)	0.1	0.9	1.0	0.5	0.4
Reticulocytes	(%)	1.9	1.6	1.8	1.6	2.0

		Animal Number				
	Units	6	7	8	9	10
WBC	(x10 <sup>3</sup> /μl)	4.6	5.4	4.4	5.9	5.0
RBC	(x10 <sup>6</sup> /μl)	7.88	7.89	8.07	8.48	8.64
Hemoglobin	(GM%)	14.3	14.3	14.7	15.3	15.2
Hematocrit	(%)	42.0	42.8	43.1	44.2	45.3
Platelets	(x10 <sup>3</sup> /μl)	907	723	605	708	667
Neutrophils	(%)	16.1	14.1	15.3	11.5	22.9
Lymphocytes	(%)	79.2	82.5	81.0	84.2	72.3
Monocytes	(%)	1.2	1.0	1.3	1.6	1.0
Eosinophils	(%)	2.3	1.2	1.6	1.5	2.2
Methemoglobin	(%)	2.7	1.6	2.5	1.7	2.4
Reticulocytes	(%)	2.2	2.2	2.4	2.0	2.3

# Hematology Values/Females

		Animal Number				
	Units	11	12	13	14	15
WBC	(x10 <sup>3</sup> /μl)	4.6	4.2	4.7	4.9	3.9
RBC	(x10 <sup>6</sup> /μl)	8.21	8.14	8.75	8.38	8.79
Hemoglobin	(GM%)	15.0	15.0	15.9	15.3	16.1
Hematocrit	(%)	44.1	44.1	45.8	44.1	46.4
Platelets	(x10 <sup>3</sup> /μl)	774	669	644	675	854
Neutrophils	(%)	13.8	17.0	16.3	13.9	13.8
Lymphocytes	(%)	82.7	79.6	80.6	82.6	81.7
Monocytes	(%)	1.3	1.2	0.8	1.0	1.2
Eosinophils	(%)	1.2	1.1	1.6	1.4	2.5
Methemoglobin	(%)	1.5	0.6	0.8	2.2	1.3
Reticulocytes	(%)	2.7	2.5	1.8	2.9	2.4

		Animal Number				
	Units	16	17	18	19	20
WBC	(x10 <sup>3</sup> /μl)	4.1	2.5	4.4	4.5	3.8
RBC	(x10 <sup>6</sup> /μl)	8.23	7.41	8.14	8.17	8.29
Hemoglobin	(GM%)	15.0	13.5	15.0	15.0	14.9
Hematocrit	(%)	43.9	39.1	43.5	43.1	44.1
Platelets	(x10 <sup>3</sup> /μl)	846	738	770	640	679
Neutrophils	(%)	19.2	15.8	16.0	19.6	19.3
Lymphocytes	(%)	77.9	80.2	79.7	76.1	77.6
Monocytes	(%)	1.3	2.2	1.2	1.4	0.5
Eosinophils	(%)	1.0	0.1	2.3	1.8	2.0
Methemoglobin	(%)	2.0	0.5	0.1	0.9	1.4
Reticulocytes	(%)	2.6	2.3	2.5	2.3	1.8

# Hematology Values/Females

		Animal Number				
	Units	21	22	23	24	25
WBC	( $\times 10^3/\mu\text{l}$ )	4.3	4.4	3.5	4.5	3.7
RBC	( $\times 10^6/\mu\text{l}$ )	8.41	8.47	8.14	8.50	8.47
Hemoglobin	(GM%)	15.4	15.4	15.2	15.6	15.6
Hematocrit	(%)	44.9	44.2	43.9	44.6	45.8
Platelets	( $\times 10^3/\mu\text{l}$ )	728	710	710	740	712
Neutrophils	(%)	13.3	17.7	22.5	18.9	21.9
Lymphocytes	(%)	82.4	78.1	73.3	76.4	73.7
Monocytes	(%)	0.8	1.5	1.8	1.7	1.4
Eosinophils	(%)	2.6	1.7	1.5	1.9	1.9
Methemoglobin	(%)	0.9	1.7	0.6	1.0	0.0
Reticulocytes	(%)	2.4	2.2	2.1	1.9	1.8

		Animal Number				
	Units	26	27	28	29	30
WBC	( $\times 10^3/\mu\text{l}$ )	5.4	5.3	3.8	5.1	5.1
RBC	( $\times 10^6/\mu\text{l}$ )	8.16	8.62	8.79	8.65	8.30
Hemoglobin	(GM%)	14.9	16.0	16.6	16.0	15.5
Hematocrit	(%)	44.0	46.7	47.6	45.6	45.0
Platelets	( $\times 10^3/\mu\text{l}$ )	792	642	671	865	628
Neutrophils	(%)	18.5	14.6	16.8	16.5	14.9
Lymphocytes	(%)	78.7	82.1	79.5	79.2	81.3
Monocytes	(%)	1.2	1.0	1.3	1.2	0.8
Eosinophils	(%)	0.7	1.5	1.3	2.1	1.9
Methemoglobin	(%)	1.0	0.4	0.6	0.1	1.0
Reticulocytes	(%)	2.0	1.7	1.5	2.3	2.4

# Hematology Values/Males

		Animal Number				
	Units	31	32	33	34	35
WBC	(x10 <sup>3</sup> /μl)	6.4	5.2	4.4	3.7	4.4
RBC	(x10 <sup>6</sup> /μl)	8.96	9.02	9.21	9.26	8.89
Hemoglobin	(GM%)	15.8	16.1	16.6	16.7	15.8
Hematocrit	(%)	47.3	46.8	49.6	49.6	47.3
Platelets	(x10 <sup>3</sup> /μl)	737	703	753	769	813
Neutrophils	(%)	25.4	22.1	24.7	16.6	34.8
Lymphocytes	(%)	69.9	74.5	71.0	79.7	63.2
Monocytes	(%)	1.3	1.3	1.6	1.1	0.7
Eosinophils	(%)	2.0	0.8	1.6	1.5	0.5
Methemoglobin	(%)	0.8	0.3	0.0	0.4	0.8
Reticulocytes	(%)	1.8	1.7	1.8	1.7	1.9

		Animal Number				
	Units	36	37	38	39	40
WBC	(x10 <sup>3</sup> /μl)	3.8	4.0	4.2	2.9	5.8
RBC	(x10 <sup>6</sup> /μl)	8.87	8.98	8.74	9.45	9.27
Hemoglobin	(GM%)	15.4	15.6	15.1	16.4	15.6
Hematocrit	(%)	44.7	46.7	46.6	48.6	47.5
Platelets	(x10 <sup>3</sup> /μl)	889	721	693	642	798
Neutrophils	(%)	17.3	15.9	18.6	27.5	13.3
Lymphocytes	(%)	79.2	81.8	78.1	68.7	84.4
Monocytes	(%)	0.9	0.6	1.3	1.2	0.7
Eosinophils	(%)	1.6	0.9	1.2	0.9	0.7
Methemoglobin	(%)	3.2	1.7	3.1	1.7	1.4
Reticulocytes	(%)	1.6	1.4	1.9	1.2	1.9

# Hematology Values/Males

		Animal Number				
	Units	41	42	43	44	45
WBC	( $\times 10^3/\mu\text{l}$ )	4.6	3.8	5.4	5.4	5.5
RBC	( $\times 10^6/\mu\text{l}$ )	9.20	9.11	8.87	9.23	9.34
Hemoglobin	(GM%)	16.1	16.0	15.6	16.0	15.9
Hematocrit	(%)	47.9	48.4	46.7	48.4	48.1
Platelets	( $\times 10^3/\mu\text{l}$ )	887	678	733	641	760
Neutrophils	(%)	18.6	19.2	20.8	18.4	14.8
Lymphocytes	(%)	78.5	77.4	74.1	76.7	82.0
Monocytes	(%)	1.0	1.3	1.3	1.3	1.4
Eosinophils	(%)	0.8	1.2	2.3	2.7	0.7
Methemoglobin	(%)	2.0	1.7	1.9	0.2	3.1
Reticulocytes	(%)	1.6	2.1	1.8	1.9	2.1

		Animal Number				
	Units	46	47	48	49	50
WBC	( $\times 10^3/\mu\text{l}$ )	4.2	3.0	5.6	4.1	4.6
RBC	( $\times 10^6/\mu\text{l}$ )	8.89	8.92	9.12	9.31	9.15
Hemoglobin	(GM%)	15.4	15.8	15.6	16.7	15.9
Hematocrit	(%)	47.1	47.5	47.0	50.9	46.3
Platelets	( $\times 10^3/\mu\text{l}$ )	779	659	615	706	659
Neutrophils	(%)	21.8	20.4	17.9	15.4	18.5
Lymphocytes	(%)	73.7	75.4	75.6	81.4	78.0
Monocytes	(%)	1.9	0.8	4.0	0.7	1.2
Eosinophils	(%)	1.6	2.3	1.2	1.1	1.0
Methemoglobin	(%)	2.3	1.1	1.4	1.8	1.6
Reticulocytes	(%)	2.0	1.6	1.9	2.0	1.6

# Hematology Values/Males

		Animal Number				
	Units	51	52	53	54	55
WBC	(x10 <sup>3</sup> /μl)	5.9	4.6	5.1	5.2	4.0
RBC	(x10 <sup>6</sup> /μl)	8.96	9.21	9.18	9.15	9.43
Hemoglobin	(GM%)	15.9	16.2	15.9	16.1	16.5
Hematocrit	(%)	47.1	49.3	47.9	48.0	50.0
Platelets	(x10 <sup>3</sup> /μl)	722	692	829	744	660
Neutrophils	(%)	19.2	26.3	31.2	21.8	12.8
Lymphocytes	(%)	76.6	71.7	64.2	73.5	83.4
Monocytes	(%)	1.6	0.9	0.9	1.4	0.8
Eosinophils	(%)	0.9	0.2	2.9	2.2	2.0
Methemoglobin	(%)	1.2	0.7	0.8	1.4	0.4
Reticulocytes	(%)	1.8	1.7	2.0	1.9	1.6

		Animal Number				
	Units	56	57	58	59	60
WBC	(x10 <sup>3</sup> /μl)	5.3	4.4	4.6	4.1	4.4
RBC	(x10 <sup>6</sup> /μl)	8.80	8.91	8.87	9.33	9.15
Hemoglobin	(GM%)	15.6	15.8	15.7	16.7	16.2
Hematocrit	(%)	46.8	47.4	46.8	50.5	47.4
Platelets	(x10 <sup>3</sup> /μl)	736	807	795	791	643
Neutrophils	(%)	28.2	23.3	23.3	18.6	33.2
Lymphocytes	(%)	67.6	72.6	72.4	78.5	62.6
Monocytes	(%)	1.2	1.9	1.4	0.9	1.1
Eosinophils	(%)	2.0	0.9	1.8	1.0	2.2
Methemoglobin	(%)	0.1	0.9	0.9	0.7	0.4
Reticulocytes	(%)	1.8	1.8	1.9	2.0	1.8

APPENDIX E

CLINICAL CHEMISTRY  
DATA

# Clinical Chemistry Measurements/Females

		Animal Number				
	Units	1	2	3	4	5
Glucose	(mg/dl)	161	112	120	93	139
BUN	(mg/dl)	22	21	18	17	19
Creatinine	(mg/dl)	0.5	0.6	0.5	0.5	0.6
Sodium	(mmol/L)	141	144	141	145	142
Potassium	(mmol/L)	4.4	4.6	4.0	4.6	4.2
AST	(U/L)	123	120	144	114	158
ALT	(U/L)	60	62	56	34	84
Phosphorus	(mg/dl)	8.8	9.9	9.7	7.9	9.3
ALK Phos	(U/L)	149	96	113	90	111
Calcium	(mg/dl)	10.4	10.5	10.6	10.1	10.7
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.1	0.0
Protein, Total	(g/dl)	5.5	5.5	5.6	5.7	5.4
Albumin	(g/dl)	3.9	3.8	4.1	4.2	4.0

		Animal Number				
	Units	6	7	8	9	10
Glucose	(mg/dl)	118	128	127	123	140
BUN	(mg/dl)	21	18	27	21	24
Creatinine	(mg/dl)	0.6	0.6	0.6	0.6	0.6
Sodium	(mmol/L)	141	141	140	141	141
Potassium	(mmol/L)	5.0	4.8	4.4	4.6	5.0
AST	(U/L)	145	180	143	177	163
ALT	(U/L)	39	56	44	50	44
Phosphorus	(mg/dl)	9.5	9.9	9.0	9.1	8.1
ALK Phos	(U/L)	110	90	130	133	157
Calcium	(mg/dl)	11.1	11.0	10.8	10.8	10.8
Bilirubin, Total	(mg/dl)	0.3	0.2	0.3	0.3	0.4
Protein, Total	(g/dl)	6.5	6.1	5.7	6.0	6.3
Albumin	(g/dl)	4.6	4.4	4.3	4.5	4.5

# Clinical Chemistry Measurements/Females

		Animal Number				
	Units	11	12	13	14	15
Glucose	(mg/dl)	123	103	128	109	139
BUN	(mg/dl)	17	20	19	16	18
Creatinine	(mg/dl)	0.6	0.6	0.6	0.6	0.5
Sodium	(mmol/L)	142	142	142	141	143
Potassium	(mmol/L)	4.4	4.4	4.3	4.6	4.9
AST	(U/L)	103	255	176	148	90
ALT	(U/L)	37	115	67	46	44
Phosphorus	(mg/dl)	8.6	9.5	9.3	9.6	9.7
ALK Phos	(U/L)	79	98	112	93	94
Calcium	(mg/dl)	11.1	10.5	10.1	10.7	10.6
Bilirubin, Total	(mg/dl)	0.2	0.2	0.2	0.2	0.1
Protein, Total	(g/dl)	6.4	6.4	6.1	6.2	5.9
Albumin	(g/dl)	4.7	4.6	4.4	4.6	4.4

		Animal Number				
	Units	16	17	18	19	20
Glucose	(mg/dl)	128	135	112	111	150
BUN	(mg/dl)	17	17	20	19	18
Creatinine	(mg/dl)	0.5	0.6	0.6	0.6	0.6
Sodium	(mmol/L)	143	142	142	141	142
Potassium	(mmol/L)	4.2	5.1	4.6	4.2	4.4
AST	(U/L)	127	109	117	124	187
ALT	(U/L)	56	41	40	43	86
Phosphorus	(mg/dl)	8.0	9.5	9.9	10.0	9.3
ALK Phos	(U/L)	92	90	103	115	85
Calcium	(mg/dl)	10.2	10.3	11.0	10.9	10.5
Bilirubin, Total	(mg/dl)	0.1	0.2	0.2	0.2	0.2
Protein, Total	(g/dl)	6.2	5.4	6.6	6.3	5.7
Albumin	(g/dl)	4.4	4.0	4.7	4.5	4.3

Clinical Chemistry Measurements/Females

		Animal Number				
	Units	21	22	23	24	25
Glucose	(mg/dl)	122	128	106	113	98
BUN	(mg/dl)	16	22	17	23	21
Creatinine	(mg/dl)	0.5	0.5	0.6	0.6	0.6
Sodium	(mmol/L)	141	141	143	141	142
Potassium	(mmol/L)	4.7	4.5	4.0	4.5	4.5
AST	(U/L)	118	117	124	140	175
ALT	(U/L)	52	47	43	43	50
Phosphorus	(mg/dl)	9.0	9.7	8.2	9.6	9.4
ALK Phos	(U/L)	98	97	87	101	113
Calcium	(mg/dl)	10.7	10.8	10.3	10.9	10.7
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.2	0.2
Protein, Total	(g/dl)	5.9	5.9	6.1	6.1	6.0
Albumin	(g/dl)	4.2	4.2	4.4	4.5	4.4

		Animal Number				
	Units	26	27	28	29	30
Glucose	(mg/dl)	147	131	128	110	121
BUN	(mg/dl)	19	18	21	21	17
Creatinine	(mg/dl)	0.5	0.5	0.5	0.6	0.5
Sodium	(mmol/L)	143	144	143	144	143
Potassium	(mmol/L)	4.8	3.8	4.9	4.2	4.3
AST	(U/L)	89	168	169	132	116
ALT	(U/L)	35	83	71	58	44
Phosphorus	(mg/dl)	9.7	8.6	10.7	9.2	9.1
ALK Phos	(U/L)	112	98	91	123	108
Calcium	(mg/dl)	10.8	10.5	10.5	10.4	9.9
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.1	0.1
Protein, Total	(g/dl)	5.7	5.8	5.9	6.0	5.6
Albumin	(g/dl)	4.1	4.2	4.3	4.3	4.1

# Clinical Chemistry Measurements/Males

		Animal Number				
	Units	31	32	33	34	35
Glucose	(mg/dl)	124	145	150	109	140
BUN	(mg/dl)	19	15	20	23	15
Creatinine	(mg/dl)	0.6	0.6	0.6	0.4	0.5
Sodium	(mmol/L)	144	139	141	144	142
Potassium	(mmol/L)	4.5	5.1	5.2	5.4	5.4
AST	(U/L)	194	139	174	QNS	127
ALT	(U/L)	103	57	92	QNS	60
Phosphorus	(mg/dl)	11.1	11.1	11.5	QNS	11.3
ALK Phos	(U/L)	163	167	156	148	151
Calcium	(mg/dl)	10.8	10.6	10.7	QNS	10.6
Bilirubin, Total	(mg/dl)	0.1	0.1	0.0	QNS	0.1
Protein, Total	(g/dl)	5.8	5.7	5.9	5.9	5.8
Albumin	(g/dl)	4.2	4.0	4.3	QNS	4.2

		Animal Number				
	Units	36	37	38	39	40
Glucose	(mg/dl)	139	181	168	153	148
BUN	(mg/dl)	17	18	19	19	22
Creatinine	(mg/dl)	0.5	0.6	0.5	0.6	0.6
Sodium	(mmol/L)	143	142	142	143	141
Potassium	(mmol/L)	5.0	5.1	5.7	5.0	4.5
AST	(U/L)	94	155	104	128	242
ALT	(U/L)	36	81	39	46	81
Phosphorus	(mg/dl)	9.6	10.6	10.3	9.3	12.0
ALK Phos	(U/L)	95	102	122	112	123
Calcium	(mg/dl)	11.2	10.9	11.4	10.8	11.1
Bilirubin, Total	(mg/dl)	0.1	0.1	0.2	0.2	0.2
Protein, Total	(g/dl)	6.7	6.3	6.6	6.2	6.5
Albumin	(g/dl)	4.8	4.5	4.8	4.5	4.7

QNS = Quantity Not Sufficient

# Clinical Chemistry Measurements/Males

		Animal Number				
	Units	41	42	43	44	45
Glucose	(mg/dl)	186	179	182	166	179
BUN	(mg/dl)	19	17	17	19	21
Creatinine	(mg/dl)	0.6	0.6	0.6	0.6	0.6
Sodium	(mmol/L)	144	143	143	143	142
Potassium	(mmol/L)	5.2	5.6	4.9	4.9	5.7
AST	(U/L)	125	110	152	164	110
ALT	(U/L)	60	46	70	58	51
Phosphorus	(mg/dl)	11.2	10.1	10.9	10.2	11.0
ALK Phos	(U/L)	117	118	128	118	127
Calcium	(mg/dl)	10.9	11.4	11.1	10.9	11.4
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.1	0.2
Protein, Total	(g/dl)	6.6	6.6	6.3	6.4	6.5
Albumin	(g/dl)	4.6	4.7	4.5	4.5	4.6

		Animal Number				
	Units	46	47	48	49	50
Glucose	(mg/dl)	138	173	215	154	144
BUN	(mg/dl)	20	19	20	20	18
Creatinine	(mg/dl)	0.5	0.6	0.6	0.7	0.5
Sodium	(mmol/L)	143	142	141	143	143
Potassium	(mmol/L)	4.8	5.4	6.0	5.8	4.4
AST	(U/L)	163	131	104	622	138
ALT	(U/L)	50	55	47	321	58
Phosphorus	(mg/dl)	12.8	10.5	11.2	12.0	10.3
ALK Phos	(U/L)	137	138	122	127	122
Calcium	(mg/dl)	11.1	10.8	11.4	11.7	10.5
Bilirubin, Total	(mg/dl)	0.2	0.1	0.1	0.2	0.1
Protein, Total	(g/dl)	6.3	6.2	6.7	6.8	6.4
Albumin	(g/dl)	4.5	4.5	4.7	4.7	4.6

# Clinical Chemistry Measurements/Males

		Animal Number				
	Units	51	52	53	54	55
Glucose	(mg/dl)	182	160	189	133	157
BUN	(mg/dl)	20	19	18	19	20
Creatinine	(mg/dl)	0.6	0.6	0.6	0.6	0.6
Sodium	(mmol/L)	142	142	142	144	143
Potassium	(mmol/L)	5.6	5.0	5.6	4.3	4.3
AST	(U/L)	94	101	96	136	392
ALT	(U/L)	38	42	42	45	181
Phosphorus	(mg/dl)	11.1	9.7	11.1	11.2	11.6
ALK Phos	(U/L)	153	120	120	151	126
Calcium	(mg/dl)	11.4	11.3	11.1	11.3	11.0
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.1	0.1
Protein, Total	(g/dl)	6.4	6.6	6.4	6.5	6.2
Albumin	(g/dl)	4.5	4.6	4.6	4.6	4.4

		Animal Number				
	Units	56	57	58	59	60
Glucose	(mg/dl)	164	178	141	158	143
BUN	(mg/dl)	23	16	20	17	20
Creatinine	(mg/dl)	0.7	0.6	0.6	0.6	0.6
Sodium	(mmol/L)	141	142	142	142	143
Potassium	(mmol/L)	4.4	6.3	5.1	5.1	5.7
AST	(U/L)	151	133	154	192	141
ALT	(U/L)	56	61	72	71	51
Phosphorus	(mg/dl)	11.1	11.8	11.6	10.8	11.9
ALK Phos	(U/L)	182	135	151	152	155
Calcium	(mg/dl)	11.6	10.8	11.1	11.3	11.2
Bilirubin, Total	(mg/dl)	0.1	0.1	0.1	0.0	0.2
Protein, Total	(g/dl)	6.3	6.1	6.3	6.5	6.6
Albumin	(g/dl)	4.4	4.3	4.5	4.7	4.8

APPENDIX F

CLINICAL OBSERVATIONS

### Clinical Observations

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07/14/93	The study started today. Initial weights were taken for food, water bottles, and animals. All animals look normal.
07/15/93	The following cage numbers had food spilled from the food bin into the cage; 6,9,13,37, and 39. The rats have played in the feeders. All animals look normal.
07/16/93	Feeders and water bottles were weighed today. All animals look normal.
07/19/93	Observed food spilled out in the following cages; 7,8,36, and 45. All animals look normal.
07/20/93	Feeders and water bottles were weighed today. New feeders and water bottles were put on the cages. The animals were weighed. All animals look normal.
07/21/93	All animals look normal.
07/22/93	Observed food spilled out in the following cages; 37,39, and 45. All animals look normal.
07/23/93	Observed food spilled out in cage 38. Feeders and water bottles were weighed today. All animals look normal.
07/26/93	All animals look normal.
07/27/93	Feeders, water bottles, and animals were weighed. Rats fasted at 2:00pm. All animals look normal.
07/28/93	Animals necropsied today. All animals look normal.

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APPENDIX G

GROSS AND  
HISTOPATHOLOGY  
DATA

## HISTOPATHOLOGY DATA

### REPORTS CODE TABLE

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable for evaluation
*	Tissues not examined/not required by protocol
1	Minimal
2	Mild
3	Moderate
4	Marked

#### Abbreviations

MF  
Inflam.

Multifocal  
Inflammation

(End of Report)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
BRAIN	# EX 5	5	0	0	0	0
SCIATIC NERVE	# EX 5	5	0	0	0	0
SPINAL CORD	# EX 5	5	0	0	0	0
SALIVARY GLAND	# EX 5	5	0	0	0	0
PANCREAS	# EX 5	5	0	0	0	0
MANDIBULAR LYMPH NODE	# EX 5	5	0	0	0	0
ZYMBAL'S GLAND	# EX 5	5	0	0	0	0
PITUITARY	# EX 5	5	0	0	0	0
ADRENALS	# EX 5	5	0	0	0	0
THYROID	# EX 5	5	0	0	0	0
PARATHYROID	# EX 5	5	0	0	0	0
TRACHEA	# EX 5	5	0	0	0	0
ESOPHAGUS	# EX 5	5	0	0	0	0
THYMUS	# EX 5	5	0	0	0	0
HEART	# EX 5	5	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1	2	3	4	5	6
NUMBER OF ANIMALS:		5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %	# %
COLON	# EX 5	5	0	0	0	0	0
JEJUNUM	# EX 5	5	0	0	0	0	0
AORTA	# EX 5	5	0	0	0	0	0
LIVER	# EX 5	5	0	0	0	0	0
Inflammation, Subacute	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
SPLEEN	# EX 5	5	0	0	0	0	0
Fibrosis	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
TONGUE	# EX 5	5	0	0	0	0	0
SKELETAL MUSCLE	# EX 5	5	0	0	0	0	0
LUNG	# EX 5	5	0	0	0	0	0
KIDNEYS	# EX 5	5	0	0	0	0	0
Regeneration, Tubular	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Degeneration, Tubular	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Mineralization, NOS	5 100.0	5 100.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Lymphocytic Infiltrates	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
URINARY BLADDER	# EX 5	5	0	0	0	0	0
STOMACH	# EX 5	5	0	0	0	0	0
DUODENUM	# EX 5	5	0	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

SEX: FEMALE

DAYS ON TEST: ALL

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1	2	3	4	5	6
NUMBER OF ANIMALS:		5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %	# %
ILEUM	# EX 5	5	0	0	0	0	0
CECUM	# EX 5	5	0	0	0	0	0
RECTUM	# EX 5	5	0	0	0	0	0
MESENTERIC LYMPH NODE	# EX 5	5	0	0	0	0	0
OVARIES	# EX 5	5	0	0	0	0	0
UTERUS	# EX 5	5	0	0	0	0	0
SKIN	# EX 5	5	0	0	0	0	0
MAMMARY GLAND	# EX 5	5	0	0	0	0	0
CLITORAL GLANDS	# EX 5	5	0	0	0	0	0
Lymphocytic Infiltrates	2 40.0	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Inflammation, Acute	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
EYES	# EX 5	5	0	0	0	0	0
Microgranuloma, Cornea	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
HARDERIAN GLAND	# EX 5	5	0	0	0	0	0
FEMUR	# EX 5	5	0	0	0	0	0
NASAL CAVITY	# EX 5	5	0	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

## PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
BRAIN	# EX 5	5	0	0	0	0
SCIATIC NERVE	# EX 5	5	0	0	0	0
SPINAL CORD	# EX 5	5	0	0	0	0
SALIVARY GLAND	# EX 5	5	0	0	0	0
PANCREAS	# EX 5	5	0	0	0	0
MANDIBULAR LYMPH NODE	# EX 5	5	0	0	0	0
ZYMBAL'S GLAND	# EX 5	5	0	0	0	0
PITUITARY	# EX 5	5	0	0	0	0
ADRENALS	# EX 5	5	0	0	0	0
THYROID	# EX 5	5	0	0	0	0
PARATHYROID	# EX 5	5	0	0	0	0
TRACHEA	# EX 5	5	0	0	0	0
ESOPHAGUS	# EX 5	5	0	0	0	0
THYMUS	# EX 5	5	0	0	1	0
Hemorrhage	0 0.0	1 20.0	0 0.0	0 0.0	1 100.0	0 0.0
HEART	# EX 5	5	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
COLON	# EX 5	5	0	0	0	0
JEJUNUM	# EX 5	5	0	0	0	0
AORTA	# EX 5	5	0	0	0	0
LIVER	# EX 5	5	0	0	0	0
Inflammation, Subacute	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
SPLEEN	# EX 5	5	0	0	0	0
TONGUE	# EX 5	5	0	0	0	0
SKELETAL MUSCLE	# EX 5	5	0	0	0	0
LUNG	# EX 5	5	0	0	1	0
Congestion	0 0.0	0 0.0	0 0.0	0 0.0	1 100.0	0 0.0
KIDNEYS	# EX 5	5	5	5	5	5
Regeneration, Tubular	1 20.0	3 60.0	1 20.0	1 20.0	1 20.0	1 20.0
Degeneration, Tubular	5 100.0	5 100.0	5 100.0	5 100.0	5 100.0	5 100.0
Mineralization, NOS	5 100.0	5 100.0	5 100.0	5 100.0	5 100.0	5 100.0
Hyaline Droplets	0 0.0	5 100.0	5 100.0	5 100.0	5 100.0	0 0.0
URINARY BLADDER	# EX 5	5	0	0	0	0
Urolith, NOS	2 40.0	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0
Hyperplasia, Epithelial	1 20.0	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0
Hemorrhage	0 0.0	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0
PROSTATE	# EX 5	5	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
STOMACH	# EX 5	5	0	0	0	0
DUODENUM	# EX 5	5	0	0	0	0
ILEUM	# EX 5	5	0	0	0	0
CECUM	# EX 5	5	0	0	0	0
RECTUM	# EX 5	5	0	0	0	0
MESENTERIC LYMPH NODE	# EX 5	5	0	0	0	0
SEMINAL VESICLES	# EX 5	5	0	0	0	0
Atrophy	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0
TESTES	# EX 5	5	0	0	0	0
EPIDIDYMIS	# EX 5	5	0	0	0	0
SKIN	# EX 5	5	0	0	0	0
MAMMARY GLAND	# EX 4	4	0	0	0	0
PREPUTIAL GLAND	# EX 5	5	0	0	0	0
Lymphocytic infiltrates	1 20.0	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0
EYES	# EX 5	5	0	0	0	0
Microgranuloma, Cornea	0 0.0	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0
HARDIAN GLAND	# EX 5	5	0	0	0	0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

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PROJECT SUMMARY

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STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

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INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

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GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
FEMUR	# EX 5	5	0	0	0	0
NASAL CAVITY	# EX 5	5	0	0	0	0
Inflammation, Chronic/Active, Peridental	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0

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Incidence Calculated by No. of Tissues Scored

(END OF REPORT)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX 5	5	0	0	0	0
SCIATIC NERVE	# EX 5	5	0	0	0	0
SPINAL CORD	# EX 5	5	0	0	0	0
SALIVARY GLAND	# EX 5	5	0	0	0	0
PANCREAS	# EX 5	5	0	0	0	0
MANDIBULAR LYMPH NODE	# EX 5	5	0	0	0	0
ZYMBAL'S GLAND	# EX 5	5	0	0	0	0
PITUITARY	# EX 5	5	0	0	0	0
ADRENALS	# EX 5	5	0	0	0	0
THYROID	# EX 5	5	0	0	0	0
PARATHYROID	# EX 5	5	0	0	0	0
TRACHEA	# EX 5	5	0	0	0	0
ESOPHAGUS	# EX 5	5	0	0	0	0
THYMUS	# EX 5	5	0	0	0	0
HEART	# EX 5	5	0	0	0	0
COLON	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
JEJUNUM	# EX 5	5	0	0	0	0
AORTA	# EX 5	5	0	0	0	0
LIVER	# EX 5	5	0	0	0	0
Inflammation, Subacute	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
SPLEEN	# EX 5	5	0	0	0	0
Fibrosis	0 0.00	1 0.40	0 0.00	0 0.00	0 0.00	0 0.00
TONGUE	# EX 5	5	0	0	0	0
SKELETAL MUSCLE	# EX 5	5	0	0	0	0
LUNG	# EX 5	5	0	0	0	0
KIDNEYS	# EX 5	5	0	0	0	0
Regeneration, Tubular	0 0.00	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
Degeneration, Tubular	0 0.00	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
Mineralization, NOS	5 1.00	5 1.00	0 0.00	0 0.00	0 0.00	0 0.00
Lymphocytic Infiltrates	0 0.00	1 0.40	0 0.00	0 0.00	0 0.00	0 0.00
URINARY BLADDER	# EX 5	5	0	0	0	0
STOMACH	# EX 5	5	0	0	0	0
DUODENUM	# EX 5	5	0	0	0	0
ILEUM	# EX 5	5	0	0	0	0
CECUM	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003			STUDY NUMBER: 93-003			
FATE: ALL			SEX: FEMALE			
DAYS ON TEST: ALL						
GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
RECTUM	# EX 5	5	0	0	0	0
MESENTERIC LYMPH NODE	# EX 5	5	0	0	0	0
OVARIES	# EX 5	5	0	0	0	0
UTERUS	# EX 5	5	0	0	0	0
SKIN	# EX 5	5	0	0	0	0
MAMMARY GLAND	# EX 5	5	0	0	0	0
CLITORAL GLANDS	# EX 5	5	0	0	0	0
Lymphocytic Infiltrates	2 0.80	2 0.80	0 0.00	0 0.00	0 0.00	0 0.00
Inflammation, Acute	0 0.00	1 0.40	0 0.00	0 0.00	0 0.00	0 0.00
EYES	# EX 5	5	0	0	0	0
Microgranuloma, Cornea	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
HARDERIAN GLAND	# EX 5	5	0	0	0	0
FEMUR	# EX 5	5	0	0	0	0
NASAL CAVITY	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX 5	5	0	0	0	0
SCIATIC NERVE	# EX 5	5	0	0	0	0
SPINAL CORD	# EX 5	5	0	0	0	0
SALIVARY GLAND	# EX 5	5	0	0	0	0
PANCREAS	# EX 5	5	0	0	0	0
MANDIBULAR LYMPH NODE	# EX 5	5	0	0	0	0
ZYMBAL'S GLAND	# EX 5	5	0	0	0	0
PITUITARY	# EX 5	5	0	0	0	0
ADRENALS	# EX 5	5	0	0	0	0
THYROID	# EX 5	5	0	0	0	0
PARATHYROID	# EX 5	5	0	0	0	0
TRACHEA	# EX 5	5	0	0	0	0
ESOPHAGUS	# EX 5	5	0	0	0	0
THYMUS	# EX 5	5	0	0	1	0
Hemorrhage	0 0.00	1 0.20	0 0.00	0 0.00	1 1.00	0 0.00
HEART	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
COLON	# EX 5	5	0	0	0	0
JEJUNUM	# EX 5	5	0	0	0	0
AORTA	# EX 5	5	0	0	0	0
LIVER	# EX 5	5	0	0	0	0
Inflammation, Subacute	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
SPLEEN	# EX 5	5	0	0	0	0
TONGUE	# EX 5	5	0	0	0	0
SKELETAL MUSCLE	# EX 5	5	0	0	0	0
LUNG	# EX 5	5	0	0	1	0
Congestion	0 0.00	0 0.00	0 0.00	0 0.00	1 1.00	0 0.00
KIDNEYS	# EX 5	5	5	5	5	5
Regeneration, Tubular	1 0.20	3 0.60	1 0.20	1 0.20	1 0.20	1 0.20
Degeneration, Tubular	5 1.80	5 2.00	5 1.80	5 1.40	5 1.20	5 1.00
Mineralization, NOS	5 1.20	5 1.60	5 1.40	5 1.20	5 1.00	5 1.00
Hyaline Droplets	0 0.00	5 2.00	5 2.20	5 1.60	5 1.20	0 0.00
URINARY BLADDER	# EX 5	5	0	0	0	0
Hyperplasia, Epithelial	1 0.20	2 0.80	0 0.00	0 0.00	0 0.00	0 0.00
Hemorrhage	0 0.00	2 0.80	0 0.00	0 0.00	0 0.00	0 0.00
PROSTATE	# EX 5	5	0	0	0	0
STOMACH	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Test, 1 Exposure  
 in Male Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
DUODENUM	# EX 5	5	0	0	0	0
ILEUM	# EX 5	5	0	0	0	0
CECUM	# EX 5	5	0	0	0	0
RECTUM	# EX 5	5	0	0	0	0
MESENTERIC LYMPH NODE	# EX 5	5	0	0	0	0
SEMINAL VESICLES	# EX 5	5	0	0	0	0
Atrophy	0 0.00	1 0.40	0 0.00	0 0.00	0 0.00	0 0.00
TESTES	# EX 5	5	0	0	0	0
EPIDIDYMIS	# EX 5	5	0	0	0	0
SKIN	# EX 5	5	0	0	0	0
MAMMARY GLAND	# EX 4	4	0	0	0	0
PREPUTIAL GLAND	# EX 5	5	0	0	0	0
Lymphocytic Infiltrates	1 0.20	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
EYES	# EX 5	5	0	0	0	0
Microgranuloma, Cornea	0 0.00	2 0.40	0 0.00	0 0.00	0 0.00	0 0.00
HARDIAN GLAND	# EX 5	5	0	0	0	0
FEMUR	# EX 5	5	0	0	0	0

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Teteryl Exposure  
in Male Fischer 344 Rats

## SEVERITY SUMMARY

STUDY ID : 93-003	STUDY NUMBER: 93-003					
FATE: ALL	SEX: MALE					
DAYS ON TEST: ALL						
GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
NASAL CAVITY	# EX 5	5	0	0	0	0
Inflammation, Chronic/Active, Peridental	1 0.60	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00

Severity Calculated by No. of Tissues Scored

(END OF REPORT)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

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TABULATED ANIMAL DATA  
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STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:

1 2 3 4 5

BRAIN	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	N	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS	N	N	N	N	N
HEART	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

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TABULATED ANIMAL DATA

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STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

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ANIMAL ID:	1	2	3	4	5
COLON	N	N	N	N	N
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N		N	N	N
Inflammation, Subacute	-	1	-	-	-
SPLEEN	N	N	N	N	N
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNG	N	N	N	N	N
KIDNEYS					
Mineralization, NOS	1	1	1	1	1
URINARY BLADDER	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:	1	2	3	4	5
MESENTERIC LYMPH NODE	N	N	N	N	N
OVARIES	N	N	N	N	N
UTERUS	N	N	N	N	N
SKIN	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N
CLITORAL GLANDS	N	N			N
Lymphocytic Infiltrates	-	-	2	2	-
EYES		N	N	N	N
Microgranuloma, Cornea	1	-	-	-	-
HARDERIAN GLAND	N	N	N	N	N
FEMUR	N	N	N	N	N
NASAL CAVITY	N	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 2

SEX: FEMALE  
-----

ANIMAL ID:	6	7	8	9	10
BRAIN	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	N	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS	N	N	N	N	N
HEART	N	N	N	N	N
COLON	N	N	N	N	N

-----  
see Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 2

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:

6 7 8 9 10

JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN	N	N	N		N
Fibrosis	-	-	-	2	-
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNG	N	N	N	N	N
KIDNEYS					
Regeneration, Tubular	-	-	1	-	-
Degeneration, Tubular	-	-	1	-	-
Mineralization, NOS	1	1	1	1	1
Lymphocytic Infiltrates	-	-	2	-	-
URINARY BLADDER	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 2

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:	6	7	8	9	10
MESENTERIC LYMPH NODE	N	N	N	N	N
OVARIES	N	N	N	N	N
UTERUS	N	N	N	N	N
SKIN	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N
CLITORAL GLANDS	N		N	N	
Lymphocytic Infiltrates	-	3	-	-	1
Inflammation, Acute	-	2	-	-	-
EYES	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N
FEMUR	N	N	N	N	N
NASAL CAVITY	N	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:	11	12	13	14	15
BRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:	11	12	13	14	15
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	*	*	*	*	*
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNG	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
OVARIES	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 3

SEX: FEMALE  
-----

ANIMAL ID:	11	12	13	14	15
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
CLITORAL GLANDS	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 4

SEX: FEMALE  
-----

ANIMAL ID:	16	17	18	19	20
BRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE  
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ANIMAL ID:

16

17

18

19

20

JEJUNUM

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AORTA

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LIVER

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SPLEEN

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TONGUE

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LUNG

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KIDNEYS

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URINARY BLADDER

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STOMACH

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MESENTERIC LYMPH NODE

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OVARIES

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Female Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 4

SEX: FEMALE

ANIMAL ID:	16	17	18	19	20
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
CLITORAL GLANDS	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:

21

22

23

24

25

BRAIN

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SCIATIC NERVE

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SPINAL CORD

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SALIVARY GLAND

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PANCREAS

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MANDIBULAR LYMPH NODE

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ZYMBAL'S GLAND

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PITUITARY

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ADRENALS

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THYROID

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PARATHYROID

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TRACHEA

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ESOPHAGUS

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THYMUS

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HEART

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COLON

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 5

SEX: FEMALE  
-----

ANIMAL ID:	21	22	23	24	25
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	*	*	*	*	*
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNG	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
OVARIES	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:

21

22

23

24

25

UTERUS

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SKIN

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MAMMARY GLAND

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CLITORAL GLANDS

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EYES

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HARDERIAN GLAND

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FEMUR

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NASAL CAVITY

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

Page 16

TABULATED ANIMAL DATA

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 6

SEX: FEMALE

ANIMAL ID:	26	27	28	29	30
BRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 6

DAYS ON TEST: ALL

SEX: FEMALE  
-----

ANIMAL ID:

26

27

28

29

30

JEJUNUM

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AORTA

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LIVER

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SPLEEN

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TONGUE

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SKELETAL MUSCLE

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LUNG

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KIDNEYS

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URINARY BLADDER

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STOMACH

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DUODENUM

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MESENTERIC LYMPH NODE

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OVARIES

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See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Female Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 6

SEX: FEMALE  
-----

ANIMAL ID:	26	27	28	29	30
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
CLITORAL GLANDS	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE  
-----

ANIMAL ID:

31

32

33

34

35

BRAIN

N

N

N

N

N

SCIATIC NERVE

N

N

N

N

N

SPINAL CORD

N

N

N

N

N

SALIVARY GLAND

N

N

N

N

N

PANCREAS

N

N

N

N

N

MANDIBULAR LYMPH NODE

N

N

N

N

N

ZYMBAL'S GLAND

N

N

N

N

N

PITUITARY

N

N

N

N

N

ADRENALS

N

N

N

N

N

THYROID

N

N

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N

N

PARATHYROID

N

N

N

N

N

TRACHEA

N

N

N

N

N

ESOPHAGUS

N

N

N

N

N

THYMUS

N

N

N

N

N

HEART

N

N

N

N

N

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 7

SEX: MALE

---

ANIMAL ID:	31	32	33	34	35
COLON	N	N	N	N	N
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	
Inflammation, Subacute	-	-	-	-	1
SPLEEN	N	N	N	N	N
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNG	N	N	N	N	N
KIDNEYS					
Regeneration, Tubular	-	1	-	-	-
Degeneration, Tubular	2	2	2	1	2
Mineralization, NOS	2	1	1	1	1
URINARY BLADDER	N			N	N
Urolith, NOS	-	P	P	-	-
Hyperplasia, Epithelial	-	-	1	-	-
PROSTATE	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	31	32	33	34	35
ILEUM	N	N	N	N	N
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N
SEMINAL VESICLES	N	N	N	N	N
TESTES	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N
SKIN	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	U
PREPUTIAL GLAND	N	N	N	N	
Lymphocytic Infiltrates	-	-	-	-	1
EYES	N	N	N	N	N
HARDIAN GLAND	N	N	N	N	N
FEMUR	N	N	N	N	N
NASAL CAVITY	N	N	N		N
Inflammation, Chronic/Active, Peridental	-	-	-	3	-

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: B

SEX: MALE

---

ANIMAL ID:	36	37	38	39	40
BRAIN	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	N	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS		N	N	N	N
Hemorrhage	1	-	-	-	-
HEART	N	N	N	N	N
COLON	N	N	N	N	N

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	36	37	38	39	40
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN	N	N	N	N	N
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNG	N	N	N	N	N
KIDNEYS					
Regeneration, Tubular	1	-	1	-	1
Degeneration, Tubular	2	2	2	2	2
Mineralization, NOS	2	2	1	2	1
Hyaline Droplets	2	2	2	2	2
URINARY BLADDER	N	N		N	
Urolith, NOS	-	-	P	-	P
Hyperplasia, Epithelial	-	-	2	-	2
Hemorrhage	-	-	2	-	2
PROSTATE	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: B

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	36	37	38	39	40
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N
SEMINAL VESICLES	N		N	N	N
Atrophy	-	2	-	-	-
TESTES	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N
SKIN	N	N	N	N	N
MAMMARY GLAND	U	N	N	N	N
PREPUTIAL GLAND	N	N	N		N
Lymphocytic Infiltrates	-	-	-	1	-
EYES	N	N	N		
Microgranuloma, Cornea	-	-	-	1	1
HARDIAN GLAND	N	N	N	N	N
FEMUR	N	N	N	N	N
NASAL CAVITY	N	N	N	N	N

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 9

SEX: MALE  
-----

ANIMAL ID:	41	42	43	44	45
BRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 9

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	41	42	43	44	45
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	*	*	*	*	*
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNG	*	*	*	*	*
KIDNEYS					
Regeneration, Tubular	-	1	-	-	-
Degeneration, Tubular	2	1	2	2	2
Mineralization, NOS	2	1	1	1	2
Hyaline Droplets	2	3	2	2	2
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 9

SEX: MALE  
-----

ANIMAL ID:	41	42	43	44	45
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
SEMINAL VESICLES	*	*	*	*	*
TESTES	*	*	*	*	*
EPIDIDYMIS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 10

SEX: MALE  
-----

ANIMAL ID:	46	47	48	49	50
BRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 10

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	46	47	48	49	50
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	*	*	*	*	*
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNG	*	*	*	*	*
KIDNEYS					
Regeneration, Tubular	1	-	-	-	-
Degeneration, Tubular	2	1	2	1	1
Mineralization, NOS	1	1	2	1	1
Myeline Droplets	2	1	2	1	2
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 10

DAYS ON TEST: ALL

SEX: MALE  
-----

ANIMAL ID:	46	47	48	49	50
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
SEMINAL VESICLES	*	*	*	*	*
TESTES	*	*	*	*	*
EPIDIDYMS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 11

DAYS ON TEST: ALL

SEX: MALE

---

ANIMAL ID:	51	52	53	54	55
IRAIN	*	*	*	*	*
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
THYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*		*	*
Hemorrhage	-	-	1	-	-
HEART	*	*	*	*	*
COLON	*	*	*	*	*

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 93-003

STUDY NUMBER: 93-003

FATE: ALL

GROUP: 11

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	51	52	53	54	55
EJUNUM	*	*	*	*	*
ORTA	*	*	*	*	*
IVER	*	*	*	*	*
IPLEEN	*	*	*	*	*
ONGUE	*	*	*	*	*
KELETAL MUSCLE	*	*	*	*	*
UNG	*		*	*	*
Congestion	-	1	-	-	-
KIDNEYS					
Regeneration, Tubular	1	-	-	-	-
Degeneration, Tubular	1	1	2	1	1
Mineralization, NOS	1	1	1	1	1
Hyaline Droplets	1	1	2	1	1
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 93-003

STUDY NUMBER: 93-003

DATE: ALL

GROUP: 11

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	51	52	53	54	55
STOM	*	*	*	*	*
ENTERIC LYMPH NODE	*	*	*	*	*
INAL VESICLES	*	*	*	*	*
TESTES	*	*	*	*	*
EPIDIDYMIS	*	*	*	*	*
IN	*	*	*	*	*
THYROID GLAND	*	*	*	*	*
EPITIAL GLAND	*	*	*	*	*
ES	*	*	*	*	*
ADIPAN GLAND	*	*	*	*	*
BLUR	*	*	*	*	*
AL CAVITY	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

---

TABULATED ANIMAL DATA

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 12

SEX: MALE

---

ANIMAL ID:	56	57	58	59	60
BRAIN	.	.	.	.	.
SCIATIC NERVE	.	.	.	.	.
SPINAL CORD	.	.	.	.	.
SALIVARY GLAND	.	.	.	.	.
PANCREAS	.	.	.	.	.
MANDIBULAR LYMPH NODE	.	.	.	.	.
ZYMBAL'S GLAND	.	.	.	.	.
PITUITARY	.	.	.	.	.
ADRENALS	.	.	.	.	.
THYROID	.	.	.	.	.
PARATHYROID	.	.	.	.	.
TRACHEA	.	.	.	.	.
ESOPHAGUS	.	.	.	.	.
THYMUS	.	.	.	.	.
HEART	.	.	.	.	.
COLON	.	.	.	.	.

---

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
 Study Number 93-003  
 14 Day Tetryl Exposure  
 in Male Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 12

SEX: MALE

ANIMAL ID:	56	57	58	59	60
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	*	*	*	*	*
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNG	*	*	*	*	*
KIDNEYS					
Regeneration, Tubular	-	-	-	-	1
Degeneration, Tubular	1	1	1	1	1
Mineralization, NOS	1	1	1	1	1
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 12

SEX: MALE  
-----

ANIMAL ID:	56	57	58	59	60
MESENTERIC LYMPH NODE	*	*	*	*	*
SEMINAL VESICLES	*	*	*	*	*
TESTES	*	*	*	*	*
EPIDIDYMIS	*	*	*	*	*
SKIN	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDIAN GLAND	*	*	*	*	*
FEMUR	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*

-----  
See Reports Code Table for Symbol Definitions

(END OF REPORT)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Teteryl Exposure  
in Male Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 7

SEX: MALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 8

SEX: MALE

---

Animal ID: 36

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 14

Reference to Necropsy Record:

THYMUS - Foci, >1mm, <5, Round, Red

Related Histopathology:

THYMUS - Hemorrhage

---

Animal ID: 37

Animal Fate: Terminal Sacrifice

Pathologist: GRO

Days on Test: 14

Reference to Necropsy Record:

SEMINAL VESICLES - Decreased in size, Severe

Related Histopathology:

SEMINAL VESICLES - Atrophy

---

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 9

SEX: MALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 10

SEX: MALE

---

No Gross Observations for any animal in this group

---

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Tetryl Exposure  
in Male Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 93-003  
FATE: ALL  
DAYS ON TEST: ALL

STUDY NUMBER: 93-003  
GROUP: 11  
SEX: MALE

Animal ID: 52  
Animal Fate: Terminal Sacrifice

Pathologist: GRO  
Days on Test: 14

Reference to Necropsy Record:  
LUNG - All lobes, Foci, <1m, >5, Round, Red

Related Histopathology:  
LUNG - Congestion

Animal ID: 53  
Animal Fate: Terminal Sacrifice

Pathologist: GRO  
Days on Test: 14

Reference to Necropsy Record:  
THYMUS - Foci, >1mm, <5, Round, Red

Related Histopathology:  
THYMUS - Hemorrhage

(REPORT CONTINUED)

Pathology Associates, Inc.  
Study Number 93-003  
14 Day Teteryl Exposure  
in Male Fischer 344 Rats

---

CORRELATION OF GROSS & MICRO

---

STUDY ID : 93-003

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 93-003

GROUP: 12

SEX: MALE

---

No Gross Observations for any animal in this group

---

(END OF REPORT)

APPENDIX H

PALATABILITY  
PRETEST DATA

## PALATABILITY PRETEST DATA

Sex	Tetryl Diet g/kg	Average Body Weight (grams) Taken at Different Weeks		Average Daily Food Intake (gms/wk/rat) Measured at Different Weeks		Average Tetryl Intake (mg/wk) Measured at Different Weeks	
		1	2	1	2	1	2
F	0	154.25	159.47	82.54	87.12	0.00	0.00
	10	149.91	138.93	67.14	74.36	653.27	698.98
	3	154.16	154.94	91.46	82.04	265.23	233.81
	1	154.77	157.89	76.13	78.60	70.03	74.67
M	0	214.43	229.89	124.70	122.75	0.00	0.00
	10	203.32	196.05	116.10	102.50	1129.65	963.50
	3	211.03	220.84	109.64	111.14	317.96	316.75
	1	213.82	229.33	117.86	111.64	108.43	106.06

**Determination of Homogeneity  
of Tetryl in the Diet**

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
Week 1				
10000	Top	10250	9730	5.36
	Middle	8990		7.56
	Bottom	9940		2.20
3000	Top	2790	2900	3.79
	Middle	2990		3.01
	Bottom	2920		0.78
1000	Top	940	920	2.29
	Middle	910		0.79
	Bottom	900		1.50
Week 2				
10000	Top	8980	9400	4.55
	Middle	9640		2.49
	Bottom	9600		2.06
3000	Top	2710	2850	5.12
	Middle	3000		5.25
	Bottom	2850		0.12
1000	Top	1010	950	7.16
	Middle	880		6.44
	Bottom	940		0.72

APPENDIX I  
CHEMICAL ANALYSES

Determination of Homogeneity  
of Tetryl in the Diet

Week 1

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
5000	Top	5670	5520	2.79
	Middle	5750		4.16
	Bottom	5140		6.95
2500	Top	2640	2330	13.0
	Middle	2080		10.6
	Bottom	2280		2.38
2000	Top	1630	1670	2.14
	Middle	1690		1.26
	Bottom	1680		0.88
1250	Top	994	1040	4.47
	Middle	1120		7.49
	Bottom	1010		3.02
500	Top	365	427	14.5
	Middle	424		0.70
	Bottom	491		15.2

Determination of Homogeneity  
of Tetryl in the Diet

Week 2

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
5000	Top	4530	4710	3.82
	Middle	4710		0.14
	Bottom	4900		3.96
2500	Top	2470	2540	2.66
	Middle	2590		1.91
	Bottom	2560		0.76
2000	Top	1830	1880	2.51
	Middle	1960		4.48
	Bottom	1840		1.96
1250	Top	1330	1190	11.5
	Middle	1030		13.8
	Bottom	1220		2.33
500	Top	456	416	9.74
	Middle	365		12.3
	Bottom	426		2.50

Stability Determination  
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Observed Concentration (mg/kg diet)			
	7 Jun 93	8 Jun 93	17 Jun 93	21 Jun 93
10000	9400	-	10700 (114)*	-
3000	2820	-	-	2850 (101)
1000	-	1020	-	950 (93)

\* Percent of original concentration.

# Average Daily Consumption of Tetryl

Week 1

Dose Group (mg tetryl/kg diet)	Males (mg/kg BW/day)	Females (mg/kg BW/day)
0	0 ± 0*	0 ± 0
5000	372.56± 13.85	354.18± 21.85
2500	169.46± 9.97	152.95± 9.15
2000	126.31± 8.83	113.10± 8.20
1250	79.82± 0.58	74.77± 2.25
500	34.01± 1.01	32.65± 1.60

\*Mean ± Standard Deviation.

# Average Daily Consumption of Tetryl

Week 2

Dose Group (mg tetryl/kg diet)	Males (mg/kg BW/day)	Females (mg/kg BW/day)
0	0 ± 0*	0 ± 0
5000	376.27± 47.38	345.34± 55.27
2500	188.49± 16.69	188.19± 4.27
2000	134.29± 3.09	128.92± 11.89
1250	85.31± 2.02	85.37± 1.72
500	30.21± 0.79	31.06± 1.98

\*Mean ± Standard Deviation.

APPENDIX J

PROTOCOL AND  
AMENDMENTS

14-DAY RANGE FINDING AND TOXICITY EVALUATION OF  
N-METHYL-N,2,4,6-TETRANITROANILINE  
IN MALE AND FEMALE FISCHER (F344) RATS

Research Protocol

Project Order (MIPR Number) #92MM2525

Tirumuru V. Reddy, Ph.D.  
Principal Investigator

F. Bernard Daniel, Ph.D.  
Co-Principal Investigator

Ecological Monitoring Research Division  
Environmental Monitoring Systems Laboratory - Cincinnati  
U.S. Environmental Protection Agency  
Cincinnati, Ohio 45268

June 24, 1993

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June 24, 1993  
Page 1

# PROTOCOL

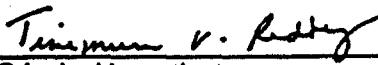
## 14 Day Range Finding and Toxicity Evaluation on

N-Methyl-N,2,4,6-Tetranitroaniline (Tetryl) in F344 Male and Female Rats

This study will be conducted in agreement with Good Laboratory Practice Standards, Environmental Protection Agency, Toxic Substances Control Act (TSCA) 40 CFR Part 792 (Federal Register, Vol 54, No. 158, August 17, 1989, pp. 34034 - 34050). All aspects of the studies will be conducted in accordance with written Standard Operating Procedures (SOP) of the performing unit and all raw data and performance documents will be maintained in agreement with GLP. An administratively separate quality assurance unit (QAU from PAI) will monitor the studies to assure adherence to good laboratory practices and the approved SOPs. Any deviation from the protocol or GLP will be noted in the raw data and reflected in the final report.

Testing Facility  
A.W. Breidenbach Environmental Research Center  
U.S. Environmental Protection Agency  
Cincinnati, OH 45268


Prime Contractor (Sponsor)  
U.S. Army Biomedical Research and  
Development Laboratory, Fort Detrick  
Frederick, Maryland 21701-5010

  
Principal Investigator  
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Date

**TITLE: 14-DAY RANGE FINDING AND TOXICITY EVALUATION OF N-METHYL-N,2,4,6-TETRANITROANILINE IN MALE AND FEMALE FISCHER (F344) RATS**

**BACKGROUND:**

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. The wastewaters discharged from trinitrotoluene (TNT) manufacturing processes contain a variety of aromatic compounds, including DNB and TNB. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, Burlinson (1980) suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct. It is also found in aquatic systems and surface soils as a by-product of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of tetryl. A recent estimate of tetryl in wastewaters generated from the production of tetryl at Joliet Army Ammunition Plant was about 36 lb/per day of each production line.

Toxicity data on these compounds are limited. The oral LD50 of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD50 of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation potentials but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs. Some of the toxicological and behavioral effects of DNB are; formation of methemoglobin, testicular degeneration and reproductive failure, and weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is rather toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin. Fetal doses (amount and route of administration are not given) of tetryl produced toxic degeneration (necrosis) in the kidneys of dogs and rabbits, and liver necrosis in dogs (not in rabbits). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Hardy and Maloof (1950) reported effects from accidental exposure of 11 people to tetryl: two died, one was disabled and eight did not detect permanent disability. They also reported irreversible liver damage, dermatitis, and upper respiratory irritation following tetryl exposure. The effects of tetryl exposure include gastrointestinal symptoms and epidermal, respiratory, nervous system, hematopoietic and circulatory injury. Atmospheric concentration of 1.5 mg/m<sup>3</sup> or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in *Salmonella* mutagenesis assay. TNB has been shown to form adducts of blood proteins and tissue DNA in rats.

## PROTOCOL

1. Study. 14-day range finding and toxicity evaluation with N-Methyl-N,2,4,6-tetranitroaniline (tetryl) in F344 male and female rats.
2. Purpose. To evaluate toxicity of tetryl when administered in the diet for 14-days and select the ideal doses for 90-day subchronic study.
3. Study Location. Andrew W. Breidenbach Environmental Research Center, U.S. Environmental Protection Agency, Cincinnati, OH 45268
4. Sponsor and Address. U.S. Army Biomedical Research and Development Laboratory, Fort Detrick, Frederick, Maryland 21701-5010
5. Principle Investigator. T.V. Reddy, Ph.D., Research Chemist Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
6. Co-Principle Investigator. F. Bernard Daniel, Ph.D, Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
7. Study Coordinator. Barry Wiechman, MS., Pathology Associates (ROW)
8. Project Manager. G.R. Olson, DVM, Ph.D., Pathology Associates (PAI)
9. Regulatory Compliance. This study is carried out according to U.S. EPA Health Effects testing guidelines (40 CFR 798) in compliance with GLP (40 CFR 792)
10. Quality Assurance. The protocol in life phase and final report will be audited by the Quality Assurance Office in accordance with SOP's at Pathology Associates, West Chester, Ohio 45069.
11. Test Material. N-Methyl-N,2,4,6-tetranitroaniline (tetryl)<sup>c</sup> (CAS#479-45-8) is supplied by the U.S. Army Biomedical Research and Development Laboratory, Ft. Detrick, Frederick, Maryland 21702. The sponsor will be responsible for the purity of the test chemical.
12. Experimental Design.

A. Selection of Dose: Toxikon Corporation, Woburn, MA 01801 has conducted acute toxicity studies on tetryl. They administered tetryl in

corn oil to rats at a single oral (Bolus) dose and observed the clinical signs for 14 days following dosing. They have reported that tetryl is nontoxic even at dose levels of 5 g/kg B.W. No unusual lesions were reported at necropsy in male and female rats. There were no established reports on the LD50 values. There are no reports on the chronic effects of tetryl in rats. Therefore, a pilot study is designed to determine the palatability.

**B. Pilot Study:** There is no information on the continuous feeding studies on tetryl; therefore, a study will be conducted for 14 days with 3 dose levels (1000, 500, and 100 mg/kg B.W.) with 5 male and female rats per group. From this study, the chemical tolerance and food consumption will be evaluated. This palatability study is essential to determine the dose levels for the 14-day toxicity study.

Four week old Fischer 344 rats with similar body weight ( $\pm 5$  g) range will be obtained from Charles River Breeding Laboratory, Portland, Michigan or Harlan (Sprague Dawley, Inc., Indianapolis, Indiana) and held for 1W for quarantine (by which time all the serological tests are evaluated). After quarantine, 20 rats with similar body weights ( $\pm 5$  g) are housed individually in clean polycarbonate shoe boxes with aspen bedding (rats are numbered with an electronic implant and all cages are sequentially numbered for identification 5 rat/each dose). Rats 1-5 are fed a 10 g/kg diet dose followed by 5. g/kg (rats 6-10) and 1 g/kg dose (rats 11-15) rats 16-20 will be given only Purina certified diet 5002 daily for 14 days. Food consumption and water consumption are recorded two times a week. Food and spoilage are taken into account while recording food consumption. Body weights are recorded once a week. During the 14 day period, the rats are watched daily for possible physical changes and toxicity. All observations are recorded and used while designing a 14-day toxicity study.

**Range Finding Experiment:** While the pilot study is in progress, 40 male and 40 female F344 rats with close body weight range ( $\pm 5$  g) will be purchased and held for 1 week for quarantine. Male and female rats, after quarantine, will be housed individually in clear polycarbonate shoe boxes in drawer rack cages with aspen bedding (San 1 Chips supplied by P.J. Murphy, Forest Products Corporation, NJ). Shoe boxes and bedding are changed along with food and water (2 times a week). Water is provided using 16 ounce bottles, stoppers and sipper tubes. At all times the animal rooms are maintained on a 12 hour light/dark cycle at 22-23°C with a relative humidity range of 40-60%.

#### **C. 1. Preparation of the Diet for the Pilot Study:**

Certified powdered Purina laboratory chow purchased from Purina labs and stored at 4°C is used. Tetryl diets are prepared once a week. Just before the diet preparation, tetryl is removed from the explosion-proof storage shelves (kept in designated carcinogen room), weighed in the carcinogen room and mixed with the powdered diet (10g/kg diet). First, 10g tetryl is mixed with 50g powdered diet and mixed and was ground in a

pestle and mortar for 15 min. Then an additional 450 g of powdered diet is added and mixed for an additional 15 min. Then the remaining diet will be added to bring the tetryl concentration to 10 g/kg; then mixed for an additional hour in a mechanical stirrer (Kitchen Aid heavy duty stand mixer, Model No. K5SS) for uniform distribution of tetryl in the diet. This is also verified by determining the tetryl concentration in the diet taken from three different depths (top, middle and bottom layer) of the final mixture. Quantitative analysis of tetryl is done by HPLC.

The premixed diet (10 g/kg) is further diluted 2 and 10 times with fresh powdered diet to obtain the desired tetryl concentration in the diet 1000, 500 and 100 mg/kg B.W. Individual diet concentrations are determined as described before. The diet feeders are changed twice a week. Tetryl concentrations are manipulated in such a way that each rat (caged individually) will receive the desired amount of tetryl. This is determined by calculating the daily average intake, followed by an adjustment of tetryl content in the diet. Dietary intake and water consumption are measured twice a week. Body weights are recorded once a week.

## 2. Preparation of the Diet for the Range Finding Experiment:

Dosing concentrations will be determined at the end of the pilot study and amended to the protocol.

D. Randomization: Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed  $\pm 2$  S $\pm$ D of the mean weight, and the mean body weights for each group of each sex will not be statistically different.

E. Justification: Rats historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies.

**F. 1. Group designation and dose levels for pilot palatability study.**

Group	No. of Rats	Sex	Tetryl Conc. in the Diet g/kg	Tetryl Target Dose mg/kg B.W.	Sacrifice Time (days)
1	5	Male	0	0	14
2	5	"	10	1000	14
3	5	"	5	300	14
4	5	"	1	100	14
5	5	Female	0	0	14
6	5	"	10	1000	14
7	5	"	5	300	14
8	5	"	1	100	14

**G. Group Designation and dose curves for Range Finding Experiment to be determined at the end of the Pilot Study and amended to the Protocol.**

**H. Analysis of the Diet for the Pilot and Range Finding Study:** The stability and the homogeneity of tetryl in the diet is determined by analyzing the tetryl content (by HPLC) in the diet, soon after diet preparation. If the tetryl concentrations vary drastically, then an alternate method of feeding (such as daily gavage) will be considered. This will be established during a palatability pilot experiment so that 14-day and 90-day studies can be carried out without any interruption.

**I. Observation of Animals:**

**1. Clinical Observations:**

Twice daily - mortality and morbidity check.

Once daily - cageside observation for obvious indications of a toxic effect; these effects will be recorded as they are observed.

Data for mortality and morbidity checks and cageside observations will be recorded on the same form. Because these are cageside animal checks, the observations will not be as specific and may not necessarily duplicate those observations recorded on body weight days when thorough physical examinations are conducted.

**2. Physical Examinations:** At each weighing interval - These observations will include, but not be limited to, changes in: skin and fur; eyes and mucous membranes; respiratory, circulatory, autonomic and central nervous systems; some motor activity and behavior.

3. Body Weight: Prior to treatment and weekly, thereafter.

4. Food Consumption: Weekly - twice.

5. Water Consumption: Weekly - twice.

J. Clinical Pathology for Range Finding Experiment:

1. Frequency: At termination.

2. Number of Animals: All animals.

K. Tests for Range Finding Experiment:

1. Hematology:

leukocyte count  
erythrocyte count  
heinz bodies  
hemoglobin

methemoglobin  
hematocrit  
platelet count  
differential leukocyte count  
reticulocyte count

2. Blood Chemistry:

glucose  
sodium  
potassium  
total protein  
albumin - phosphorus  
calcium  
total bilirubin

urea nitrogen  
creatinine  
aspartate aminotransferase  
alanine aminotransferase  
alkaline phosphatase

L. Termination:

1. Unscheduled Sacrifices and Deaths: Necropsies, by trained personnel using procedures approved by board-certified pathologists, will be conducted on all moribund animals and on all animals that die during the range finding experiment.

2. Sacrifice: After 14 days of treatment on the range finding experiment, all surviving animals will be weighed, anesthetized with sodium pentobarbital, and exsanguinated. Necropsies will be conducted on each animal in a random order to eliminate bias by trained personnel using procedures approved by board-certified pathologists. Animals will be fasted for 12 hrs before sacrifice.

A pathologist will be readily available for consultation (further participation by a pathologist is available).

3. Tissues will not be collected from animals on the Pilot Study.

M. Postmortem Procedures for the Range Finding Experiment:

**1. Gross Necropsy:** The necropsy will include examination of:

external surface  
all orifices  
cranial cavity  
carcass

external surface of the brain (at necropsy) - cut surfaces of the brain  
thoracic, abdominal and pelvic cavities and their viscera  
cervical tissues and organs

**2. Organ Weights:** For each terminally sacrificed animal, the following organs (when present) will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

brain	lungs
liver	thymus
spleen	testes with epididymides/ovaries
kidneys	heart
adrenals	

**3. Tissue Preservation:** The following tissues (when present) from each animal will be preserved in 10% neutral buffered formalin:

skin	ileum
mandibular lymph nodes	colon
mesenteric lymph nodes	cecum
mammary glands	rectum
thigh muscle	liver
sciatic nerve	pancreas
sternum with marrow	spleen
femur with marrow	kidneys
larynx	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs and bronchi	prostate
heart and aorta	testes, including epididymis
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity and nasal turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord

**N. Histopathology for the Range Finding Experiment:**

1. Following necropsy, a list of all gross lesions recorded will be submitted to the project officer at U.S. Army Biomedical Research and Development Laboratory for his evaluation and for any additional histopathology other than those described below.

Histopathological evaluations are to be done on the following tissues from all the animals (male and female from the highest dose group and untreated controls). The tissues examined under a light microscope are as follows:

cerebrum	pancreas
cerebellum	cecum
trachea	colon
thyroid	rectum
parathyroid	stomach
esophagus	skeletal muscle
salivary gland	sciatic nerve
harderian gland	tongue
heart	skin
aorta	mammary gland
lung	nasal region
thymus	sternum
spleen	femur
mesenteric lymph node	vertebrae
liver	spinal cord
kidneys	adrenals
urinary bladder	pituitary
duodenum	eye(s)
jejunum	Zymbal's gland
ileum	

MALE  
accessory sex glands  
epididymis  
testes

FEMALE  
uterus  
ovaries

An average of 12 slides will be prepared for each rat covering all the tissues shown above (3 or 4 tissues are fixed on each slide). A total of 240 slides from 20 rats (5 male and 5 female from high dose 14-day study and 5 rats each from control group) from the 14-day study will be examined. Based on the results from dose group tissues from other doses, groups will be examined as needed. Following completion of each study, all raw data wet tissues, paraffin blocks and slides will be placed in the EPA storage facility.

#### 0. Final Report:

Four months after the termination of the in-life phase of the range finding experiment, a final report which includes the following information (as appropriate) will be prepared and submitted to the Sponsor:

#### 1. Experimental Design and Methods:

## 2. Results:

mortality  
clinical observations  
body weights  
food and liquid consumption  
clinical pathology tests

organ weights and organ/body  
weight ratios  
gross pathology  
histopathology

Statistical Evaluation for the Range Finding Experiment:

Stat-view computer software will be used for statistical analysis.

Dunnet's t-test will be used for comparing the treatment groups.

Kruskal-Wallis rank sums will be used, if needed, to examine the differences among the treatment groups and Wilcoxon rank sum test will be used to analyze pairwise differences between the control and each dose group.

Amendment 1  
for  
United States Army Study 93-003  
14 DAY RANGE FINDING AND TOXICITY EVALUATION OF N-METHYL-N,2,4,6-  
TETRANITROANILINE IN FISCHER (F344) RATS

For  
United States Army  
Biomedical Research and Development Laboratory  
Fort Detrick  
Frederick, MD 21701-5010

The purpose of Amendment 1 is: 1) provide study start and completion dates, 2) provide dose levels, and 3) describe diet preparation.

1. Page 10, Add the following: P. Study Schedule:

Study Start Date: July 14, 1993  
Necropsy Date: July 28, 1993  
Study Completion Date: October 28, 1993

Reason: These dates were not included in the protocol originally.

2. Page 6, G - Add the following:

Group Designation and dose levels for 14 Day Range Finding study

Group	# Rats	Sex	Tetryl Target Dose (mg/kg b.w.)	Tetryl Conc. in Diet (mg/kg)
1	5	Female	0	0
2	5	Female	500	5000
3	5	Female	250	2500
4	5	Female	200	2000
5	5	Female	125	1250
6	5	Female	50	500
7	5	Male	0	0
8	5	Male	500	5000
9	5	Male	250	2500
10	5	Male	200	2000
11	5	Male	125	1250
12	5	Male	50	500

Reason: Not included in protocol originally.

3. Page 5, C.2 - Add the following:

The preparation of the diet for the 14 Day Range Finding study is the same as the pilot study except 5 g of tetryl is mixed with the diet instead of 10 g. Also, the premixed diet is diluted 50, 60, 75 and 90 percent with powdered diet instead of 50 and 90 percent.

Reason: Not included in protocol originally.

Amendment 1 Approval

U.S. Army Medical Research and  
Development Laboratory  
Fort Detrick  
Frederick, Maryland 21701-5010

AW Breidenbach Environmental Research Ctr  
US Environmental Protection Agency  
Cincinnati, Ohio 45268

 7-2-93  
G. Reddy, Ph.D., Sponsor Date

 7-26-93  
T.V. Reddy, Ph.D., PI Date

 7-21-93  
Willie Fox, M.A., QA Date

Deviations from GLP's and Protocol

1. Clinical observations were performed twice daily but recorded once daily.

Tirumuru V. Reddy  
Tirumuru V. Reddy, Ph.D.

## DISTRIBUTION LIST

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